Certificate

This is to certify that the following work titled, 'Pathology of choledochal cyst in adults and children: a prospective analysis of cases from 2010-2012,' is an original bonafide work by Sudhindra J, resident in General Surgery at CMC Vellore (2010-2013) in part fulfillment of the requirements of the MS General Surgery branch I exam to be held in April 2013.

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Acknowledgements

I would like to place on record my gratitude to the following without whom, this work would not have been possible:

Dr. V. Sitaram (Head of HPB Surgery), guide, mentor and role model: for all that he has taught me and the support during the study as well as during the course.

Drs. Philip Joseph (HPB Surgery) and Anna Pulimood (Pathology): for sagely counsel during the difficult initial months and the enthusiasm in making this work see the light of day.

Drs. Frederick Vyas and Ravish Sanghi (HPB Surgery): for the advice in constructing the study, the operative work and encouragement.

Dr. Sudipta Sen and the Pediatric surgery team for their ready support and participation.

Drs. Anu Eapen (Radiology), Banumathi Ramakrishna, Rekha Pai (Pathology) and Joe Fleming (Biochemistry): for carrying the varied aspects of the study on their shoulders.

Drs Anand Bharatan and Dhiraj John (HPB Surgery): for the operative work and the intra-operative photographs.

Drs Deepak Burad and Veena Jayaraj (Pathology): for incorporating the study protocol in their reports and for the photographs of slides.

Mr Arun Nehru and Mr Dhananjayan (Molecular pathology): for completion of K-ras analysis at short notice.

My co-registrars: for the attention to thesis details in the wards and operation theatres.

Mr Simon (Pathology): for extracting all slides and blocks from the Pathology archives in record time.

Drs Tulasi and Hanumantha Rao (aunt and uncle): for all the encouragement during the study and the course.

Dr Kruthika Narayan (cousin): for always being ready to help with difficult to procure articles, notwithstanding the time of the day.

CMC Vellore and all my teachers, for making this study and this course a reality.

All the patients and parents of child patients: for cheerful participation in spite of the burden of illness. Their fortitude makes our problems seem small.

My parents: for their unconditional support at every stage in life, especially when the going got difficult.

And last, but not in the very bit least, God for his abundant grace.

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Paper ID	293532918
Paper title	Thesis
Assignment title	Medical
Author	Sudhindra 22101254 M.S. General Surgery
E-mail	sudhindra.j@gmail.com
Submission time	16-Dec-2012 12:48PM
Total words	8517

First 100 words of your submission

Pathology of choledochal cysts in adults and children: a prospective analysis of cases from 2010 to 2012 A dissertation submitted in partial fulfilment of the requirements of M.S (Branch-I) General Surgery examination of the Tamilnadu Dr. MGR Medical University, Chennai to be held in March 2013 Contents 1. Introduction 2. Aims of the study 3. Review of Literature 4. Materials and methods 5. Results 6. Discussion 7. Conclusions 8. Bibliography 10. Annexure Introduction Choledochal cyst is a condition characterized by abnormal, aneurismal dilatation of a segment of the bile duct, usually in the extra-hepatic location.(1) Its incidence varies from 1 in 0.1-0.15 million in the Western population...

Abstract

TITLE OF THE ABSTRACT : Pathology of choledochal cysts in adults and children
DEPARTMENT : General surgery
NAME OF THE CANDIDATE : Sudhindra J
DEGREE AND SUBJECT : MS General Surgery
NAME OF THE GUIDE : V Sitaram

OBJECTIVES: Describe the objectives of your study (maximum 30 words)

To compare the clinical, radiological and pathological characteristics of choledochal cysts in adults and children and describe differences if any.

METHODS: Explain the clinical and statistical methods used (maximum 100 words)

All patients with choledochal cyst presenting to General Surgery IV, HPB Surgery and Pediatric surgery between November 2010 and May 2012 were included.
-Informed consent was obtained from all participants.
-At laparotomy, bile was obtained from the common duct for measurement of Amylase and Lipase
-Intra-operative cholangiogram was performed thereafter.
-The presence of dysplastic changes and K-ras mutation in the epithelium was noted in the cyst at histopathological examination.
-Results were analysed to study the association between type of cyst/ junction and the junction length on one hand with the bile Amylase level/ pathological changes/ K-ras mutation in the lining epithelium on the other.

RESULTS: Summarise the findings and conclusions of your study (maximum 90 words)

1. Choledochal cysts were commoner in females.
2. Common presenting complaints were pain, vomiting and cholangitis.
3. Coexisting pathology included gallstones, choledocholithiasis and biliary stricture.
4. The commonest cyst type was I in adults and IVA in children.
5. Ultrasonography and MRCP were the common diagnostic modalities used.
6. Long common channel was associated with higher serum/ bile amylase and lipase.
7. MRI and intra-op cholangiogram showed good correlation; MRI identified the common channel better.
8. Children showed higher bile amylase levels.
9. K-ras mutation was uncommon (2/36).
10. Complications and positive bile cultures were commoner in adults.

Pathology of choledochal cysts in adults and children: a prospective analysis of cases from 2010 to 2012

A dissertation submitted in partial fulfilment of the requirements of M.S (Branch-I) General Surgery examination of the Tamilnadu Dr. MGR Medical University, Chennai to be held in March 2013.

Contents

Introduction

Choledochal cyst is a condition characterized by abnormal, aneurismal dilatation of a segment of the bile duct, usually in the extra-hepatic location.(1) Its incidence varies from 1 in 0.1-0.15 million in the Western population to 1 in 1000 in Asia.(2) It is divided into 5 morphological types (2) of which types I and IVA are most common.

Choledochal cysts are associated with abnormal junction of the pancreatic and common bile ducts outside the wall of the duodenum. This leads to the loss of the protective action of the sphincter of Oddi in the wall of the duodenum leading to reciprocal reflux of bile and pancreatic secretions. This predisposes to recurrent cholangitis, pancreatitis, stricture formation and choledocholithiasis secondary to stasis. Repetitive inflammation of the bile duct ultimately produces malignant transformation of the biliary epithelium secondary to several cycles of epithelial breakdown and repair.(3) This theory is supported by the occurrence of several premalignant epithelial changes (dysplasia, biliary intra-epithelial neoplasia) as well as molecular changes (K-ras and p53 mutations) in the cyst epithelium.(3) Complete excision of the cyst and hepatico-enterostomy is therefore recommended to disconnect the bile duct from the pancreatic duct and remove the diseased segment of the bile duct that could predispose to malignancy in the future.(4)

This prospective study intended to compare the following features in adults and children presenting with choledochal cyst over an 18 month period to a tertiary care centre in South India:

-Clinico-pathological profile,

-findings on imaging,

-operation performed and

-post operative course.

Aims of the study

1. To classify patients who present with choledochal cyst into anatomical types as described by Todani.(5)

2. To study the prevalence of pancreatico-biliary maljunction (PBM) in these patients, particularly with reference to the presence of long common channel (2).

3. To compare magnetic resonance cholangiopancreatography (MRCP) with intra-operative cholangiogram (IOC) in the detection of cyst type and PBM.

4. To study the association between PBM and elevated amylase level in the bile in the common bile duct. (6)

5. To identify the presence of pathological changes in the bile duct associated with pancreatic reflux namely, hyperplasia, metaplasia, dysplasia and biliary intra-epithelial neoplasia (BilIN).

6. To identify the presence of K-ras mutation in the epithelium of the cyst wall and factors that predict its occurrence.

7. To correlate bile culture with post operative sepsis and to see if there is a relationship between the two.

8. To describe differences (if any) between children and adults with respect to the above mentioned aspects of choledochal cyst.

Review of literature

Choledochal cyst is a defined as segmental, aneurismal dilatation of the bile duct, most commonly in its extrahepatic portion.(1) In such individuals, the diameter of the common bile duct exceeds 10 mm.(3) Its incidence is varied and has been variously described as being as rare as 1 in 100,000 to 150,000 in the Western population to being as common as 1 in 1000 in the Asian population for reasons that are not understood. (2) The frequency of various types of choledochal cyst in literature is:

50%–80% type I,

2% type II,

1.4%–4.5% type III,

15%–35% type IV and

20% type V.(2)

The first classification system for choledochal cysts was proposed by Alonso Lej and colleagues in 1959.(7) This system classified extrahepatic biliary dilatation into 3 types. Todani and colleagues incorporated intrahepatic biliary dilatation into this system to propose a modified classification that is widely accepted and used today.(5)

Type I and IV are the commonest cyst types encountered. Type I cysts are subdivided into 3 groups: IA- where there is dilatation of the entire extrahepatic bile duct,

IB- where the dilatation of the bile duct occurs distal to the cystic duct-common hepatic duct confluence and

IC- where dilatation extends from the pancreatico-biliary junction to the intra-hepatic biliary tree. Recently, a ’ type ID’ cyst has been described in which the cystic duct is dilated in addition to the hepatic and common bile ducts giving it a bicornuate appearance.(1)

Type II cysts are diverticuli that arise from the common bile duct while type III are those in which the intraduodenal portion of the common bile duct is dilated. Due to the similarity to ureterocoele, this variety has been christened as 'choledochocoele.' These have been further subdivided into 5 types based on the relationship of the cyst to the pancreatic duct and ampulla of Vater.(8) Some authors have questioned the inclusion of choledochocoele as a type of choledochal cyst due to differences in clinical presentation, pancreatic duct anatomy and propensity to develop biliary tract cancers when compared with other types of choledochal cyst.(9)

Type IV cysts are multiple and have been divided into 2 types:

IVA- where the dilatation involves both the extra hepatic as well as the intra hepatic bile ducts and IVB- where there are multiple dilated segments in the extra hepatic bile duct alone; the latter is seen as a 'string of beads' on imaging.

Type V cysts exhibit cystic dilatation confined to multiple segments of the intrahepatic bile ducts. This type is also referred to as, 'Caroli's disease' or 'communicating cavernous ectasia.' In these, the extrahepatic bile duct measures less than 3 cm in diameter.(10)

Form fruste is a cyst type characterized by an abnormal junction of the common bile and pancreatic ducts with long common channel and distal common bile duct stenosis in the absence of biliary dilatation. Patients with this cyst type present with the classical symptoms of pain and jaundice.(11)

Other cyst types that have been described include combination of type I and II cysts (diverticulum arising from type IC cyst)(12) and isolated cystic duct dilatation ('type VI' choledochal cyst).(13)

Pathogenesis of choledochal cyst

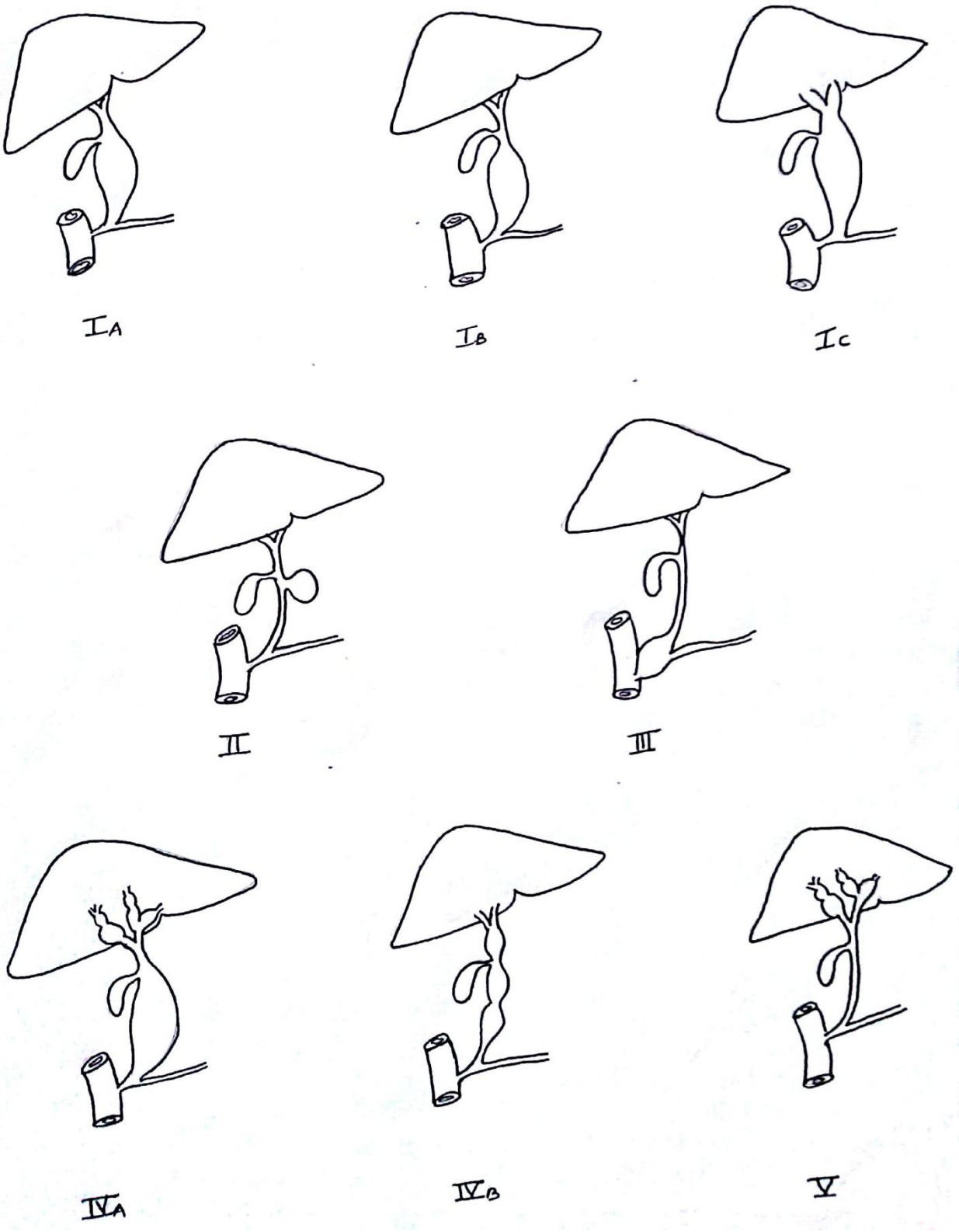
Several theories have been proposed to explain the development of choledochal cysts. These include the following:

1. Babbitt's theory: choledochal cysts are mostly associated with an abnormal junction of common bile duct and main pancreatic ducts; they unite outside the wall of the duodenum. This leads to mixing of pancreatic secretions and bile which causes activation of pancreatic enzymes and alters bile acids. Due to the higher pancreatic ductal pressures, there is reflux of these irritant contents into the common bile duct which leads to inflammation and weakening of the wall causing dilatation of the common bile duct.(14) Davenport and Basu contended that increased pressure in the common channel as opposed to that at the ampulla, contributed to pancreatico-biliary reflux.(15) This theory has been corroborated by the finding that bile duct amylase levels are higher in patients with choledochal cyst than in controls.(16) Trypsin and Phospholipase A2 levels were also found to be elevated in bile aspirated from choledochal cysts. Biliary epithelium which is dysplastic in PBM, secretes Enterokinase(17) which activates Trypsinogen to Trypsin which then activates Phospholipase A2. (18)This in turn contributes to the inflammatory breakdown and weakening of the bile duct wall. The higher the amylase level, the younger the age of onset of symptoms and greater the degree of epithelial dysplasia in the bile duct.(2)
2. Another theory states that all choledochal cysts are a result of anomalous development of the bile duct secondary to increased epithelial proliferation in the cannulation period in biliary development.
3. Davenport and Basu (15) suggested that choledochal cysts are analogous to Hirschsprung's disease in pathogenesis. All neonatal choledochal cysts they studied were cystic and exhibited fewer ganglia as well as neurons in the wall. Aganglionosis possibly contributed to distal obstruction and proximal dilatation.
4. The above theories do not explain the development of other cyst types such as II, III and V. Type II cysts are believed to be duplication cysts of the bile duct and type III cysts are believed to

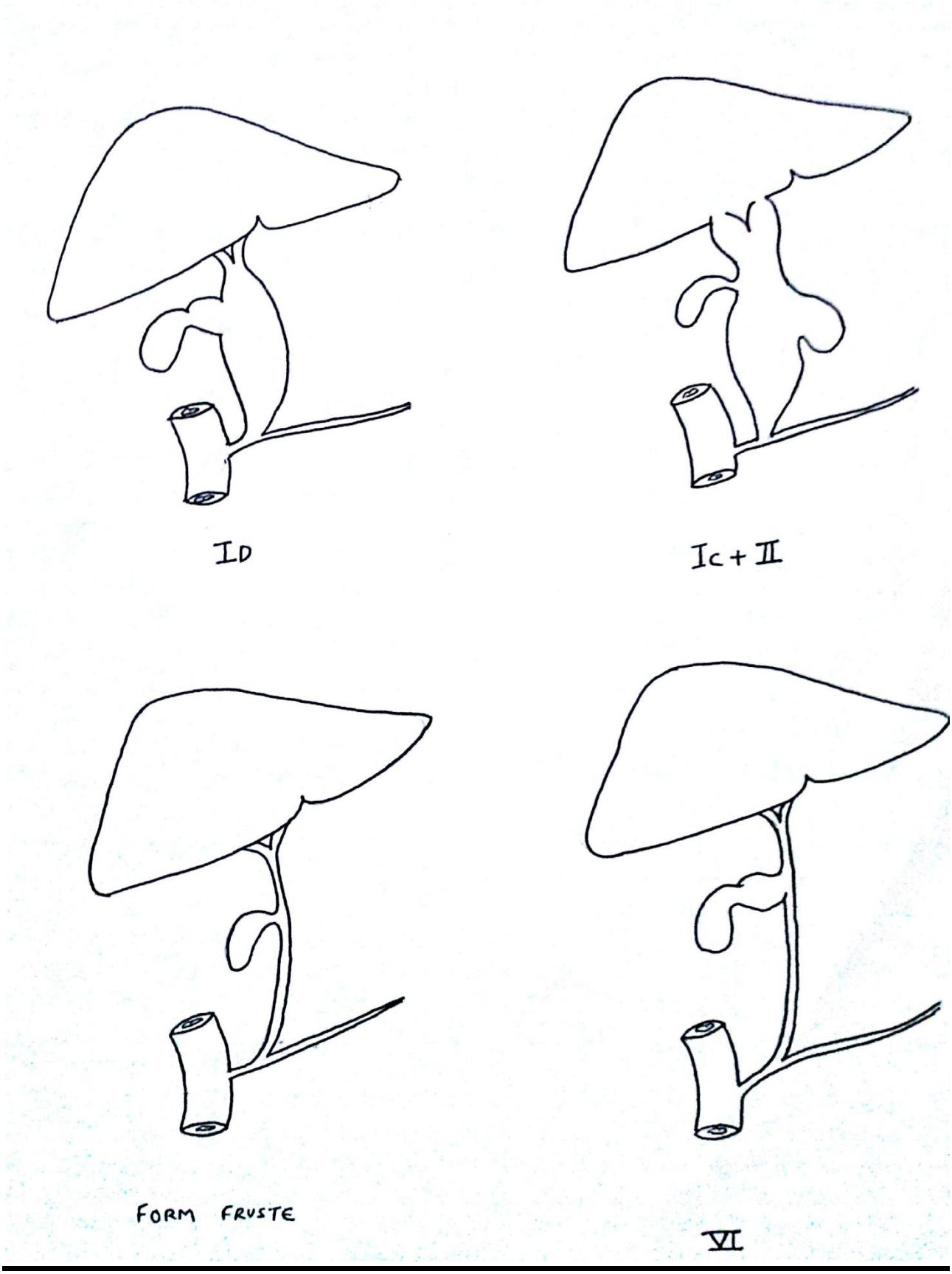
occur as a result of ampullary obstruction or sphincter of Oddi dysfunction.(2) Some authors believe that type III cysts are duplication cysts of either the distal bile duct or duodenum.(19)

5. Type V cysts on the other hand, are believed to result from an arrest in duct plate modelling in hepatic development. In the 12^{th} week of intra-uterine life, the bile duct epithelial cells form a duct plate with two layers around the branches of the portal vein which, by selective resorption and remodelling, develops into the biliary tree. Large duct development arrest leads to the manifestation of Caroli's disease while arrest at the ductule level contributes to intrahepatic cyst formation with fibrosis (Caroli's syndrome). (2,20)

Todani classification (5)



Other choledochal cyst types(2)



Pancreatico-biliary maljunction

Choledochal cysts are associated with PBM in 50-80 % of cases.(2) PBM is defined as the junction of bile and pancreatic ducts outside the wall of the duodenum, beyond the influence of the sphincter of Oddi.(21) However, this excludes abnormal junction due to acquired

factors such as papillitis, common bile duct stones and neoplasms.(22) The definition of PBM is not clear. The following definitions have been published so far:

i) Common channel >15 mm.(24, 25)

ii) Common channel >20 mm, perpendicular union of ducts/ both.(25)

iii) Common channel 6 mm or more outside the duodenal wall.(26)

iv) Common channel >15mm + bile amylase >10,000 U/L.(27)

The prevalence of PBM is also varied and ranges from 1% in Europe(28), 0.9-1.5%(3) in Japan to 8.7% in Taiwan(29) among patients who underwent ERCP for complaints that could be attributed to biliary pathology. In India, Jesudason et al reported the incidence of PBM in choledochal cyst to be 14%.(30)

PBM is not seen only in choledochal cyst. The presence of PBM in the absence of biliary dilatation has been documented in 22% of Japanese patients registered under the Japanese Study Group on

pancreatico-biliary maljunction (JSPBM).(3)

The theories that explain the development of PBM are also varied. According to one theory, there is an arrest in the migration of the junction into the wall of the duodenum which produces the

characteristic morphology of a common channel. Another theory suggests that PBM is a result of misarrangement of the pancreatico-biliary duct system where the common bile duct joins the ventral branch of the pancreatic duct.(31) Komi et al proposed a system to classify PBM based on the angle of junction of the common bile duct with the main pancreatic duct:

Type I- Junction at right angles.

Type II- Junction at an acute angle.

These are further classified as subtypes A- where the common channel is of normal calibre and B- where the common channel is dilated.

Classification as type III is based on the configuration of the major and minor pancreatic ducts:

Type III A: Both minor and major pancreatic ducts are patent and separate.

Type IIIB: Minor duct patent, major duct absent distal to junction with common bile duct with no connection between the ducts.

Type IIIC1- Patent minor duct, major duct distal to junction with common bile duct replaced by fibrous cord connecting with the minor duct.

Type IIIC2- Both ducts patent, of normal calibre and communicating with each other.

Type IIIC3- Both ducts patent, dilated and communicating with each other.

The common channel may also be classified based on whether the common bile duct joins the pancreatic duct (c-p type) or vice versa (p-c type).(32)

Classification of PBM(33)

IA

IB

IIA

IIB

IIIA

IIIB

IIIC1

IIIC2

IIIC3

Long common channel

The length of the common channel in PBM patients is usually greater than 1.87 cm.(3) Misra and Dwivedi defined the length of a long common channel to be greater than 8 mm.(34) However, Jona et al defined the long channel to be >10 mm in adults and >4mm in infants.(35) We should remember that there may be variations in the length of the common channel as a result of age, physical structure and radiological magnification used.(22)

The problems associated with a long common channel are manifold:

i) Carcinoma of the biliary tract, especially if >15 mm and even if >8 mm.(3,34)

ii) Carcinoma pancreas.(3)

ii) Choledochal dilatation of the bile duct.(34)

iii) Pancreatitis, if the channel is long and its diameter greater than that of the stone.(34)

PBM has been associated with various pathological states such as choledochal cyst, gall bladder (GB) cancer, cholangiocarcinoma, GB adenomyomatosis, biliary pancreatitis, non biliary pancreatitis, hilar cholangiocarcinoma, cholelithiasis and pancreatic cancer.(36)

In another study, it was observed that the incidence of K-ras mutation in cholangiocarcinoma is higher in those with long common channel. There is a sequential increase as one moved from proximal to distal extrahepatic bile duct. This suggests that long common channel has a bearing on biliary carcinogenesis possibly due to pancreatic reflux.(37) Factors that affect the degree of reflux include length and degree of dilatation of the common channel.(38)

Biliary carcinoma

It was believed that the frequency of gall bladder cancer is high in patients with PBM and normal calibre common bile duct while in those with choledochal cyst, cholangiocarcinoma predominates.(39)

However, the JSPBM registry statistics in 2009 revealed that 12.9% of PBM patients with choledochal cyst exhibited biliary cancer (8.8% GB and 5.2% bile duct) while in those with a normal bile duct, the incidence was 38.5% (36.5% gallbladder and 4.0% bile duct).

There was no difference between the incidences of cholangiocarcinoma in those with choledochal cyst when compared with those who had normal calibre bile ducts. When compared with the normal population in Japan, the incidence of bile duct cancer was 285 times higher in those with PBM.(3) Patients with PBM developed biliary cancers almost a decade earlier than the general population with a progressive increase in incidence with age.(40)

From India, Misra and Dwivedi reported the incidence of gall bladder cancer in those with a long common channel to be as high as 67% (8 out of 12 patients).(34) In another study which compared biliary cancers in pediatric and adult patients with PBM it was found that there were no malignancies in the pediatric group. However, in adults, 13.3% of cystic type choledochal cysts demonstrated cholangiocarcinoma. GB cancer frequencies were as follows: cystic (6.7%), spindle-like (33.3%) and non dilated (80.0%). Bile duct cancers were found to be more prevalent before the age of 40 years while the incidence of gall bladder cancers increased after that in patients with PBM associated with choledochal cyst.(40) This suggested the necessity for early excision of the common bile duct in those with choledochal cyst and cholecystectomy in those with normal calibre common bile duct, before the evolution of biliary carcinoma.(41)

Pathogenesis of biliary cancer in PBM

The precise mechanism of biliary carcinogenesis in PBM is not fully understood. Many events take place and could contribute to the development of biliary cancer.

1. When the common bile duct and pancreatic duct unite outside the wall of the duodenum, the function of the sphincter of Oddi is lost. There is mutual regurgitation of bile and pancreatic secretions and stagnation in the GB and the dilated bile duct.

2. Pancreatic isoenzymes undergo activation when mixed with Enterokinase secreted by the dysplastic biliary epithelium.(17)

2. The action of Enterokinase on pancreatic isoamylases leads to the production of phospholipase A2 and lysolecithin which are cytotoxic.(34)

4. Bile acids are deconjugated leading to increased levels of secondary bile acids within the bile duct. Deoxycholic and cholic acid are structurally similar to Methylcholantrene which is a carcinogen.(3)

5. Pancreatic reflux is also believed to lead to lipid peroxidation and DNA oxidation in the biliary epithelium as evidenced by the presence of 4 hydroxy-2-nonenal-modified protein, a lipid peroxidation product and 8-hydroxy-2'-deoxyguanosine, an oxidative DNA base modified product in the gall bladders of patients with PBM.(42)

These changes result in epithelial injury and chronic inflammation within the bile duct. Repeated cycles of damage and repair of biliary epithelium leads to hyperplasia, metaplasia, dysplasia and carcinoma. This is brought about by DNA damage, mutation of tumour suppressor as well as oncogenes and acceleration of the cell cycle.(3)

Analysis of the contents of the bile duct from patient s with PBM revealed mutagenicity in 50% by both the Ames as well as the spore rec test which respectively signify the mutagen's ability to bring about frameshift mutations and DNA damage.(18, 43) These findings were echoed by Kato

et al who used the Bacillus subtilis test to demonstrate mutagenicity.(44) The mutagens were thought to be amino acids with a molecular weight between 1500 and 3000.(18) Reciprocal reflux in PBM also predisposes to cholangitis, pancreatitis, bile duct stones and biliary carcinoma.(45) An interesting observation concerning reflux is that in patients with dorsal duct dominance (pancreas divisum), the bile amylase level and the incidence of gall bladder cancer was found to be lower. This was probably because of an alternative pathway of drainage of bile through the duct of Santorini as opposed to the main pancreatic duct of Wirsung and consequently, decreased reflux of pancreatic enzymes into the common bile duct from the main pancreatic duct.(46) (47)

Histopathological changes

The incidence and grade of epithelial hyperplasia is greater in the non cancerous epithelium of patients with PBM whether carcinoma gall bladder is present or not. (46, 47) Papillary hyperplasia is believed to be a precursor for gall bladder cancer and the risk was found to increase with age.(49) Epithelial hyperplasia (especially high grade) was more common in those with PBM and undilated bile duct than in those with a dilated duct. Non PBM epithelium was usually not associated with hyperplasia or dysplasia.(50) Direct correlation was observed between the degree of reflux (i.e., gall bladder amylase level) and the degree of epithelial hyperplasia in the gall bladder.(51) Hyperplasia and cell proliferation was especially more prevalent in the gall bladders of patients with P-C type of junction as compared to those with C-P type. This was attributed to greater likelihood of reflux and associated inflammatory changes in those with P-C type of PBM.(32) Reflux of pancreatic secretions into the bile duct in PBM is believed to lead to the sequence of chronic inflammation, hyperplasia, metaplasia, dysplasia and carcinoma (26). Another observation was that larger the choledochal cyst, more intense the inflammation.(51)

Molecular changes

1) Proliferating cell nuclear antigen labelling index which used to measure cellular turnover, was higher in the non cancerous biliary epithelium of patients with PBM (irrespective of the duct diameter) in comparison with controls.(52)

2) Ki-67, which is a marker for cellular kinetic activity, was found to be over-expressed in both cancerous as well as non-cancerous gall bladder epithelium in PBM (irrespective of duct diameter). The highest levels are found in gall bladder cancer associated with PBM and there was an association between Ki-67 over-expression and high grade epithelial dysplasia.(50)(45)

3) Non neoplastic epithelium in PBM showed a high frequency of mucin core protein MUC1 expression. This was also observed in areas of dedifferentiation and invasion in the cancerous epithelium. This is suggestive of an altered cellular phenotype and increased potential for cancer in PBM.(53)

4) Cyclo-oxygenase 2 (COX-2) and vascular endothelial growth factor (VEGF) are over-expressed in the biliary epithelium of patients with PBM. These contribute to carcinogenesis by their anti-apoptotic and angiogenic actions respectively.(54)

5) Levels of 8 hydroxy 2 deoxyguanosine, which is a by product of oxidative DNA base modification, is higher in gallbladders of patients with PBM than in controls. This shows that oxidative DNA damage occurs in PBM which may predispose to cancer.(42)

Genetic changes

1) Bcl 2, which is an inhibitor of apoptosis, was found to be expressed in the mitochondrial membrane of the cancerous as well as non-cancerous gall bladder epithelium in patients with PBM. However, it was not expressed in the cancerous or non-cancerous gall bladder epithelium in

sporadic gall bladder cancer. Bcl 2 expression is probably an early event predisposing to biliary carcinogenesis in patients with PBM.(55)

2) Telomerase activity, which predisposes to cancer, is increased in both cancerous as well as non-cancerous gall bladder epithelium in patients with PBM. However, it was not increased in non-cancerous gall bladder epithelium of sporadic gall bladder cancer.(55)

3) Micosatellite instability (MSI) was found in 85.7% of hyperplastic lesions associated with PBM in Nagai's study which shows that PBM may predispose to malignancy.(56)

4) Inactivity of p53 leads to cell cycle dysregulation, impaired DNA repair and suppression of apoptosis. This in turn results in increased cellular proliferation that leads to malignant change. Various alterations including mutation, over-expression and loss of heterozygosity have been described with respect to p53.(3) P53 genetic alterations are believed to be a late event in biliary carcinogenesis and some authors have reported their occurrence only in carcinoma of the biliary tract.(56) Funabiki et al reported over-expression of p53 protein in 27.8% and 35.7% of gallbladder and bile duct epithelia of patients with PBM but without cancer. This frequency was 20% in the non-cancerous portion of the biliary tract in patients with PBM with biliary cancer and 57% in the cancerous portion.(3) Similarly, p53 mutations were found in 60% of gallbladder and 100% of bile duct cancers of patients with PBM. These figures were 45% and 64.3% respectively in those without PBM.(3) The frequency of loss of heterozygosity is very high in both cancerous as well as non cancerous epithelium of patients with PBM with gall bladder cancer.(3)

5) P14-ARF mutations lead to loss of inhibition of p53-mdm2 interaction and subsequent dysfunction in p53 tumour suppression pathway. These mutations were frequent not only in the cancerous but also the non cancerous epithelium in PBM.(3)

PBM and K-ras mutation

K-ras mutations are common in the biliary epithelium of patients with PBM. They are chiefly in codon 12 of exon 1. The reports with respect to its incidence and association with biliary pathology from different investigators vary. (3) In one study K-ras mutations were found in hyperplastic, metaplastic and dysplastic epithelium of patients with PBM. No mutations were observed in the non cancerous epithelium of patients without dilated CBD. (57) Tomono et al reported the presence of K-ras mutation at codon 12 in not only bile duct/ gall bladder cancer associated with choledochal cyst, but also in epithelial atypia.(58) K-ras mutation was found only in those patients with PBM in a study on stage I gall bladder (33). The frequency of K-ras mutations in PBM related biliary pathology is higher than that in PBM unrelated pathology of the biliary tree. Hidaka et al demonstrated a higher incidence of K-ras mutation in patients with cholangiocarcinoma who also had a long common channel. There was a sequential increase in mutation frequency when one progressed from the proximal to the distal biliary tree; this supports the reflux theory of mutagenesis.(37) In another study, K-ras mutation was more prevalent in the gall bladders of patients without bile duct dilatation as compared to the bile ducts of patients with choledochal cyst.(39). A few investigators however, did not find any association between K-ras mutation and benign biliary tract lesions in patients without PBM. K-ras mutation is therefore, believed to be an early event in biliary carcinogenesis.(60, 61)

Clinical features

Most patients present before the age of 10 years. Two thirds present with two out of the classical triad of pain, jaundice and abdominal mass. While neonates present with jaundice and abdominal mass, older patients present with nausea, vomiting, pain, fever and jaundice. These symptoms are attributable to reciprocal reflux and cholangitis/ pancreatitis. The dilated bile duct leads to bile stasis, protein plug precipitation, stone formation, inflammatory scarring and further obstruction.

Pancreatitis could result from one of three causes- obstruction by stones, protein plugs or distal stricture. Protein plug formation occurs due to precipitation of protein rich inflammatory exudates or hypersecretion of mucin by dysplastic epithelium.

Patients with intrahepatic stasis (type IC, IVA, V) present with recurrent cholangitis, intrahepatic abscess and ultimately, secondary biliary cirrhosis. This in turn leads to portal hypertension and even acalculous cholecystitis in some patients.

Type 3 cysts may be asymptomatic or present with gastric outlet obstruction due to direct duodenal obstruction or intussusception.

About 1-2% may present with biliary peritonitis secondary to rupture. Rupture is believed to occur because of inflammation induced mural fragility in combination with increased pressure within the duct or the abdomen.

Diagnosis

1. Ultrasonography

The most commonly used imaging modality in the diagnosis of choledochal cyst is ultrasonography. All cyst types except III and V appear as cystic lesions at the porta which are in continuity with the bile duct. This differentiates them from pancreatic pseudocysts, hydatid cysts and biliary cystadenomas.(61) Ultrasonography is inexpensive, readily available in most instances, non-invasive and is non time consuming. There is no exposure to radiation involved. Its sensitivity has been reported to be 71-97% in literature.(62) However, ultrasonography is limited by body habitus, bowel gas, overlying structures and is operator dependant; it does not offer the anatomic detail that is obtained from MRI/ ERCP. Endoscopic ultrasound (EUS)overcomes many of these limitations and allows for visualization of the intrapancreatic bile duct.(63, 64)

2. Magnetic resonance cholangiopancreatography (MRCP)

This is now considered to be the gold standard in Hepatobiliary imaging. Bile and pancreatic secretions have different signal intensities as compared to the surrounding soft tissue which helps in image creation. However, blood, stones, protein plugs and air in the bile duct could interfere with image acquisition. Its sensitivity and specificity ranges from 90-100%.(64) However, MRCP is poor at imaging the pancreatico-biliary junction, tortuous ducts and stones/ ducts smaller than 5mm.(66, 67)

Administration of secretin prior to imaging may help by dilating the pancreatic duct due to increased pancreatic secretion.(67) MRI does not involve exposure to ionizing radiation, does not have complications of cholangitis/ pancreatitis, is operator independent and offers excellent anatomic detail. However, visualization of junction is poor and therapeutic procedures cannot be

carried out. Gadoxetic acid enhanced functional MRI has recently been described as a tool to demonstrate reflux in pancreatico-biliary maljunction.(68)

3. Cholangiography

Cholangiography involves visualization of the biliary tract after the injection of radio-opaque contrast into the biliary tree. This could be accomplished either via the ampulla at endoscopy (ERCP), the intrahepatic bile ducts percutaneously (PTC) or intra-operatively, most often through the cystic duct (IOC). It is useful in:

1. Delineating biliary tract anatomy including that of the pancreatico-biliary junction before an operation.
2. Identification of filling defects (stones/ tumours).(69)
3. In performing therapeutic procedures such as sphincterotomy and stone extraction.

However, pitfalls include high risk of cholangitis and pancreatitis which increases with the contrast load used in large cysts.(67)

Patients with choledochal cyst are at increased risk due to the presence of common channel, dysfunctional sphincter and dilated duct. Other problems include exposure to ionizing radiation(70), operator dependant results, little use in the post operative setting due to distal (intestinal) run off(71), technical difficulties in cases where the ampulla is scarred due to inflammation(70) and the need for anaesthesia in children(72).

4. Computerized tomography (CT)

CT is useful to study the intra-hepatic bile duct architecture, to demonstrate cyst continuity with the bile duct, identify malignant change within the cyst as well as study the distal common bile duct and pancreas.(73) Computed tomographic cholangiography could add further to anatomic detail obtained from CT. Virtual endoscopy of the bile duct and 3 dimensional reconstruction using cholangiography and spiral CT have also been used for this purpose and also in evaluating the anastomosis after the operation.(69) However, CT involves exposure to radiation and nephrotoxic contrast.

5. Hepatobiliary Imino Diacetic Acid scan (HIDA scan)

Technetium^{99} HIDA scan is primarily used to demonstrate bile duct continuity. This can differentiate biliary atresia from choledochal cyst in children by the absence of contrast entry into the small bowel in the former. HIDA can also identify cyst rupture and post op anastomotic leak by the entry of the isotope into the peritoneal cavity. However, anatomic detail, especially of the intrahepatic ducts is poor, which limits its sensitivity to 67% for type IVA cysts.(62)

Treatment

Treatment of choledochal cyst depends on the type of cyst and the clinical situation in which it is encountered. This has undergone several modifications in the last 80 years. In 1924, McWhorter described cyst excision followed by hepatico-jejunostomy.(74) However, this was not used for a long period of time due to several complications. Several other operations had been described including cyst marsupialisation, cystorraphy and cysto- enterostomy. These have been abandoned due to morbidity, mortality and the risk of malignant transformation in the future which is seen in as many as 30% of those who undergo internal drainage procedures.(75)

Therefore, the standard of care today is excision of choledochal cyst from hepatic hilum to pancreatic duct with Roux-en-Y hepatico-enterostomy.(76) This separates the bile duct from the main pancreatic duct thereby preventing the reflux of pancreatic juice into the biliary tract and also removes the damaged portion of the bile duct with malignant potential.(4) If the cyst cannot be completely excised, the epithelium needs to be denuded or destroyed with alcohol or iodine.

Hepatico-jejunostomy has a 92% success rate and a 7% complication rate as opposed to a 42% complication rate with hepatico-duodenostomy. The latter procedure carries with it the risk of bile reflux induced gastritis, esophagitis and hilar malignancy.(78, 79) However, there have been other reports to the contrary which make the choice unclear.(79)

Various modifications of hepatico-enterostomy have been described. These include:

1. End to end hepatico-jejunostomy. (No redundant jejunal pouch).
2. Short Roux limb based on the distance between hepatic hilum and umbilicus. (Avoids complications of redundant jejunum).
3. Wide stoma at hilum (3 cm or more) by extending incisions along the lateral walls of the hepatic duct. (Avoids anastomotic stricture).
4. Appendiceal conduit between hepatic duct and jejunum. (Reduced cholangitis due to high follicle content in the appendix).

5. Chicago-Beijing procedure (jejunal conduit between hepatic duct and duodenum with spur valve at duodenal anastomosis- reduced pancreatic reflux).

6. Laparoscopic/ robotic hepatico-enterostomy (shorter hospital stay, comparable complication rate, decreased blood loss).

7. Hepatico-cutaneous jejunostomy (dilatation of high intra hepatic strictures and stone extraction).

Post operative complications following hepatico-enterostomy include bile leak, pancreatitis and bowel obstruction in the immediate post operative period. Late complications include anastomotic stricture, malignancy (0.7-6%), cholangitis, bile duct stones, pancreatitis and peptic ulcer. Intra-operative cholangioscopy may help in the removal of stones, protein plugs and debris which may prevent post operative biliary obstruction/ cholangitis. Also, the junction can be traced which may prevent inadvertent pancreatic duct injury during resection. Some authors have advocated pre-operative biliary stent placement in patients who have symptomatic common bile duct stones.(80)

Type II cysts could be removed by simple excision while type III cysts may be treated by ERCP and sphincterotomy if symptomatic as opposed to surgical resection of the intra-luminal portion of the cyst.(81)

Type IV cysts call for hepatico-enterostomy with a wide hepatic stoma to facilitate bile drainage.(82) Following this, resolution of intrahepatic dilatation has been reported. Hepatico-cutaneous jejunostomy (facilitates hepatic stone extraction/ lithotripsy) and segmental hepatectomy (focal dilatation with recurrent complications) may be indicated in some type IVA cysts.(83)

Caroli's disease is treated by hepatectomy if segmental or orthotopic liver transplantation if diffuse.(84)

Form fruste cysts can be treated with either cholecystectomy alone or along with excision and hepatico-enterostomy as there are arguments that favour both procedures in literature.(84)

Patients who present with biliary peritonitis following rupture are managed with emergent celiotomy, washout and external drainage of the perforation followed by definitive procedure at a second sitting. Rupture is commonly seen in pregnant women due to stasis secondary to biliary

hypomotility as well as increased intra-abdominal pressure secondary to the gravid uterus and labour.(85)

Coexistent malignancy mandates excision of the extra-hepatic bile duct, adjoining liver and the draining lymph nodes. However, less than 10 % of malignancies are resectable at presentation.(86)

Finally, the definitive operative procedure is best performed in early neonatal period because beyond this, the incidence of hepatic fibrosis and post operative complications increases.(87)

Materials and methodology

-All patients with choledochal cyst presenting to General Surgery IV/ Department of HPB Surgery/ Department of Pediatric Surgery between Nov 2010 and May 2012 were included in the study.

-As per institutional policy, children were defined as those less than 15 yrs of age and all those aged 15 years or more were included in the adult bracket.

-Pre-operative evaluation of the biliary tree was carried out using ultrasonography and/ or MRCP with CT abdomen as per unit policy.

-Informed consent was obtained from all adults and the assent form was administered to children (if appropriate) following which consent was obtained from the nearest relative present with the child before the operation.

-At laparotomy, bile was aspirated from the common bile duct for measurement of amylase and lipase levels.

-The bile amylase and lipase were measured under the supervision of a senior biochemist using a standardized colorimetric method using the substrate 4-nitrophenyl-maltoheptaoside.(88)

-Intra-operative cholangiogram (IOC) was performed after the collection of bile sample.

-IOC and MRCP images were reviewed by a senior radiologist and the cyst type and junction length were determined from them.

-After excision, the proximal and distal ends of the excised cyst were labelled and subjected to histopathological examination.

-The presence of the following changes in the cyst lining epithelium, were noted: epithelial hyperplasia, intestinal metaplasia, dysplasia and intra-epithelial neoplasia. The findings were verified by a senior HPB pathologist.

-One slide with the above mentioned epithelial change(s) was selected for each patient and the area of interest was marked.

- The corresponding block was subjected to tissue, DNA extraction and rt-PCR to detect the presence of K-ras mutation in codon 12.

-Results were analysed to study the association between type of cyst/ junction and the junction length on one hand with the bile amylase and lipase level as well as pathological changes/ K-ras mutation in the lining epithelium on the other. The Chi square test was used in all instances to ascertain statistical significance except in the comparison of MRI and IOC, where correlation coefficient was employed.

Results

Age distribution (chart I)

There were 17 children and 25 adults who were treated for choledochal cyst in the period between Nov 2010 and May 2012 in General Surgery IV/ Department of HPB Surgery / Department of Pediatric Surgery. All of these were elective admissions.

Gender distribution (chart II)

There was a female preponderance in both in both adults (18 out of 25) as well as children (14 out of 18). The female to male ratio among adults was 2.57:1 while among children it was 3.5:1 (0.67).

Clinical presentation (chart III)

The most common presenting features were pain (29%), jaundice (23%), vomiting (18%) and cholangitis (12%) in children. In adults, these were pain (96%), vomiting (48%) and jaundice/ cholangitis (20%). Children tended to present with jaundice more commonly than adults while pain was not as prominent a symptom in them. (90, 91).

Associated pathology

Table 1

	Adult	Paediatric
Bile duct stones	5	2
Bile duct stricture	1	1
Pancreatitis	1	2
Gallstones	6	1
Hepatolithiasis	1	0

The common coexisting pathological conditions in adults and children treated for choledochal cyst is as shown in table no: 1. In addition to the above, biliary cirrhosis, portal hypertension, liver abscess and several developmental anomalies have been reported in literature. The developmental anomalies include atresia of the anus, duodenum and colon, pancreas divisum, pancreatic hypoplasia/ arteriovenous malformation, heterotopic pancreatic tissue, absence of portal vein, familial adenomatous polyposis (FAP), multiseptate gall bladder, ventricular septal defect, aortic hypoplasia and OMENS plus syndrome. (2)

Serum bilirubin (chart IV)

All patients were investigated with liver function tests and serum amylase/ lipase. Most patients had low serum total bilirubin level (<2 mg/dL). However, there was a greater fraction of children with high serum bilirubin than adults (p=0.2).(91)

Serum alkaline phosphatase (chart V)

All children had elevated alkaline phosphatase values (>125 IU/L) while most adults had low alkaline phosphatase levels (p=0.03 for 300U/L cut-off). This could be explained by increased bone formation in children.

Pre-operative imaging (chart VI)

Ultrasonography and MRI were the commonest investigations used to diagnose choledochal cyst. While the former was more common in children, the latter predominated in adults. This reflects the changing trend of preferring MRI/ MRCP over ERCP in the diagnosis of biliary pathology.

Serum amylase vs. channel length (chart VII)

Among children, a greater number with a long common channel had a high serum amylase level (>100 IU/L) (p=0.76). However, among adults, the number with high serum amylase was equal to those with a low serum amylase, irrespective of the presence of a long common channel (p=1). Hyperamylasemia is seen in those with a common channel especially if > 10 mm in length due to the greater chance for pancreatico-biliary reflux.(92)

Cyst type (chart VIII)

While type I was the most common cyst type in adults, in children it was type IVA (p=0.33). In one child, the type of cyst could not be identified on imaging (IOC).

Junction length and long common channel (chart IX)

Junction lengths were divided into three groups based on length (34):

- <8mm

-8 and 15mm and

->15 mm

Most adults had junction lengths that were either less than 8 or more than 15 mm. In case of children, most fell into the 8-15 mm bracket. Twelve out of 25 adults and 5 out of 17 children had long common channel (>10 mm) (p=0.91).(3)

Cyst type vs. junction length (chart X and XI)

One view is that choledochal cysts are congenital in nature. Therefore, both the cyst and the common channel may be a result of the same developmental anomaly and the cyst type may correspond to the junction length.(93) There appears to be no difference in the prevalence of long common channel when type I cysts were compared with type IVA cysts in adults (p=0.55). In children, the long common channel was more prevalent in type I cysts (p=0.196).

Junction length vs. bile amylase and lipase (charts XII and XIII)

Among adults, a greater fraction of those with a short common channel had low bile amylase level (<200 IU/L) while the converse held true for those with a long common channel (p=0.12). Among

children, the results were less clear with equal numbers in the low amylase level group (p=0.81). However, only those with a long common channel had amylase levels in excess of 50,000 IU/L. Thus, longer the channel length, the greater is the level of bile amylase which is in keeping with reports from literature.(38) A similar trend was observed when bile lipase levels were studied in relation to junction length. However, the results were less clear in children with equal numbers in the low and intermediate (10,000-50,000 IU/L) groups in those with a short common channel. However, the recurrent theme seemed to be that in those with a long common channel, there were a greater proportion of patients who had bile lipase levels in excess of 50,000 IU/L.

MRI vs. intra-operative cholangiogram (chart XIV)

There were 10 adults whose cyst types and junction lengths could be made out both on MRI and IOC. There was good correlation between MRI and intra-operative cholangiogram in identifying the junction length. There was no discrepancy in the type of cyst identified. (Correlation coefficient- 97.17). MRI is non invasive without exposure to radiation. It is a viable alternative to traditional imaging modalities in the study of biliary pathology. Intra-operative cholangiogram is user dependant and technically more demanding as compared to MRI. Moreover, it does not contribute to pre-operative planning and exposes both the patient and the surgical team to radiation. However, it is inexpensive as compared to MRI.

Junction length on MRI and IOC (chart XV)

The pancreatico-biliary junction and its length were better seen on MRI- in 81% of children and 100% of adults. In IOC it was 16% of children and 47% of adults. This emphasizes the operator dependant nature of IOC. Therefore, although there was good correlation in the measurement of junction length between MRI and IOC, the former is better in identifying junction length and is therefore, the investigation of choice between the two.

Bile amylase and lipase vs. age (chart XVI and XVII)

The adult group showed an equal number of patients who had bile amylase level below 10,000 IU/L and those with a level >10,000. In comparison, the pediatric group had a greater fraction in the >10,000 group (71%). This was in keeping with the reports in literature that in those who were symptomatic and therefore, presented to the surgeon at a younger age, the bile amylase level was higher (p=0.89).(51) Bile amylase level correlates with the symptoms and the degree of dysplasia in the bile duct.(2) A similar trend was observed when lipase levels in bile were compared with age.

Bile culture (chart XVIII)

Bile culture was obtained intra-operatively in most patients (14 out of 18 children and 25 out of 25 adults). All the cultures (14) were sterile in children. Although most (13) adults had no growth on culture, 4 had monomicrobial and 7 had polymicrobial culture reports. However, there was no relationship between the presence of organisms in culture and the post operative course/ complication.

Histopathology and K-ras mutation

Chronic inflammation, hyperplasia, intestinal metaplasia and dysplasia were commonly observed. The first change was uniformly seen in all patients. Biliary intra-epithelial neoplasia was less common (2 patients). There was no significant difference in pathological changes observed between adults and children. Similarly, there was no correlation of histopathology with bile amylase level/ cyst type/ channel length. K-ras mutation was observed in only two patients (1 adult and 1 child). This was probably because of low epithelial yield due to extensive denudation in the cysts and consequent non-representative samples.

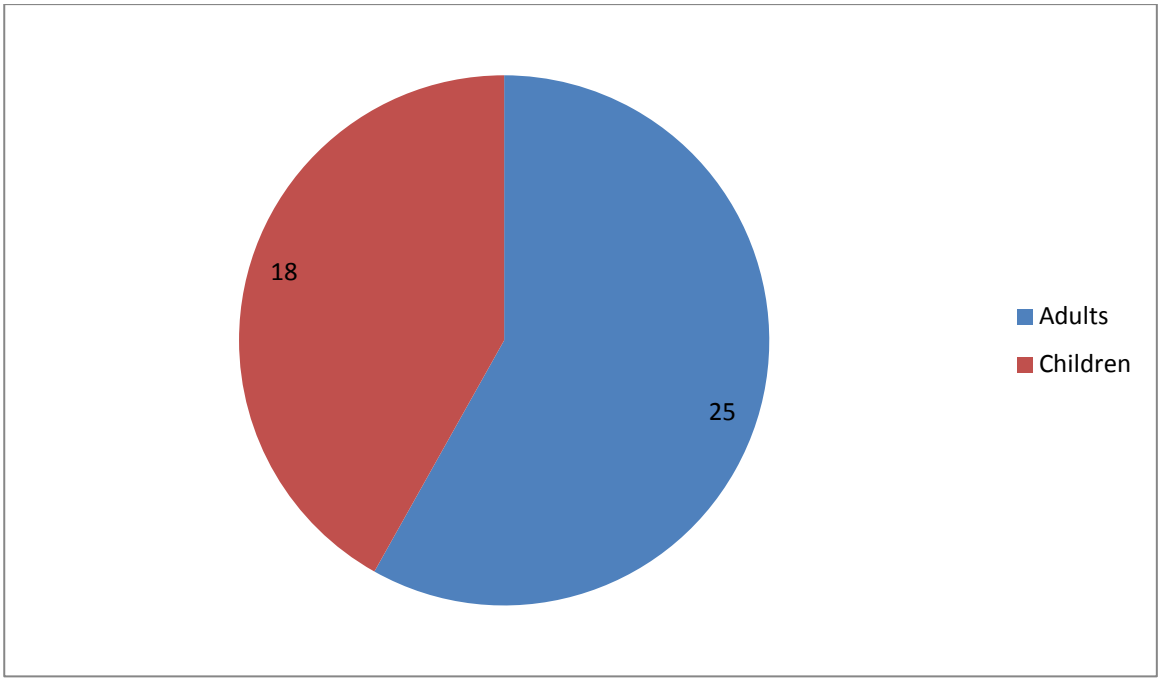
Operation performed (chart XIX)

The commonest operation in adults was open hepatico-jejunostomy following excision of choledochal cyst. In children, the numbers were almost equally distributed between open hepatico-jejunostomy and open hepatico-duodenostomy. One adult underwent radical cholecystectomy for carcinoma gall-bladder associated with choledochal cyst while in one child; laparoscopic hepatico-duodenostomy was performed.

Complications (chart XX)

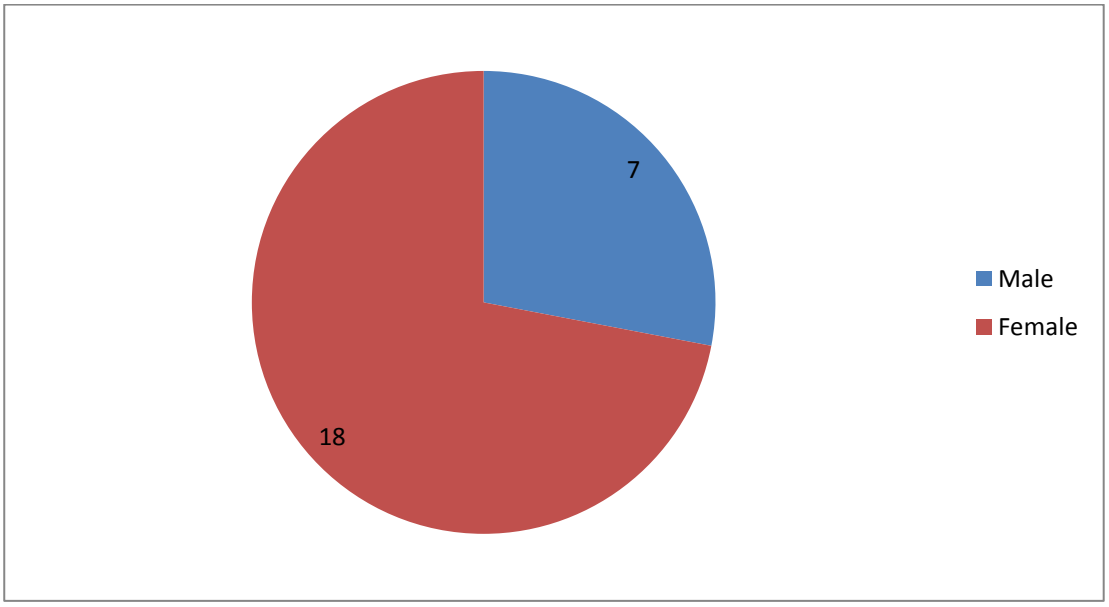
There were no post operative complications observed in children during the period of this study. However, complications were seen in 60% of the adults operated. The most common complication was bile leak (9 patients). One patient with bile leak required re-exploration, washout and trans-anastomotic stent placement and another required pigtail drain placement for intra-abdominal collection. The other 7 settled on conservative treatment. The other complications include wound infection (2 patients), septicemia (1 patient), anastomotic leak requiring reoperation (1 patient), gastric distension (1 patient) and secondary hemorrhage (2- bleed into drain, 1- melena). Patients with secondary hemorrhage resolved without intervention.

I) Age distribution

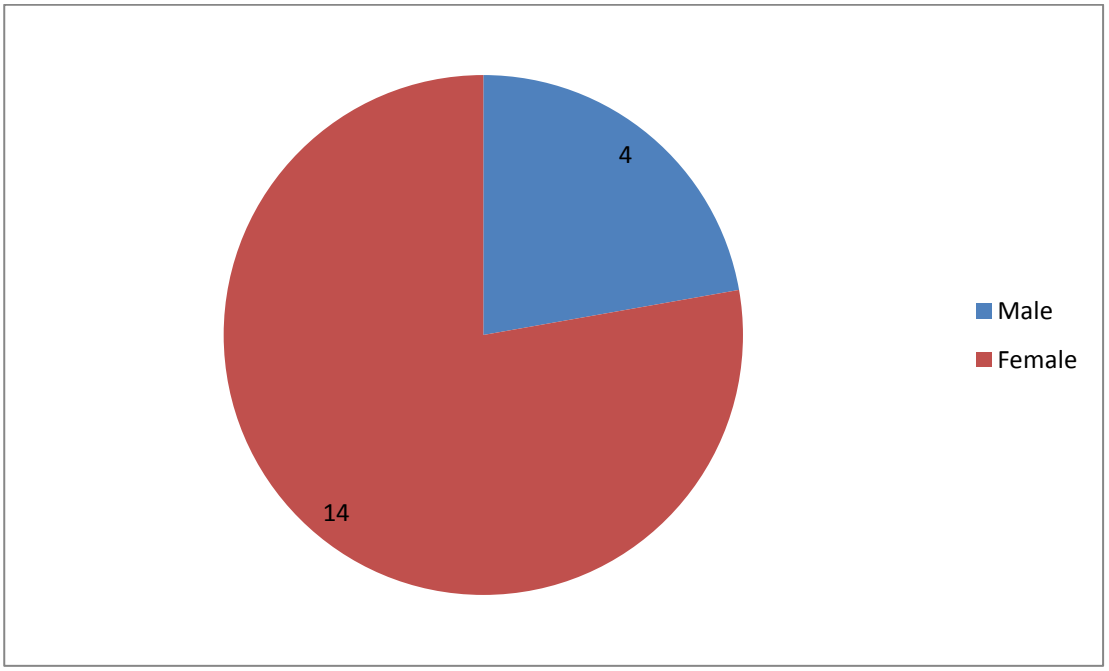


II) Gender distribution

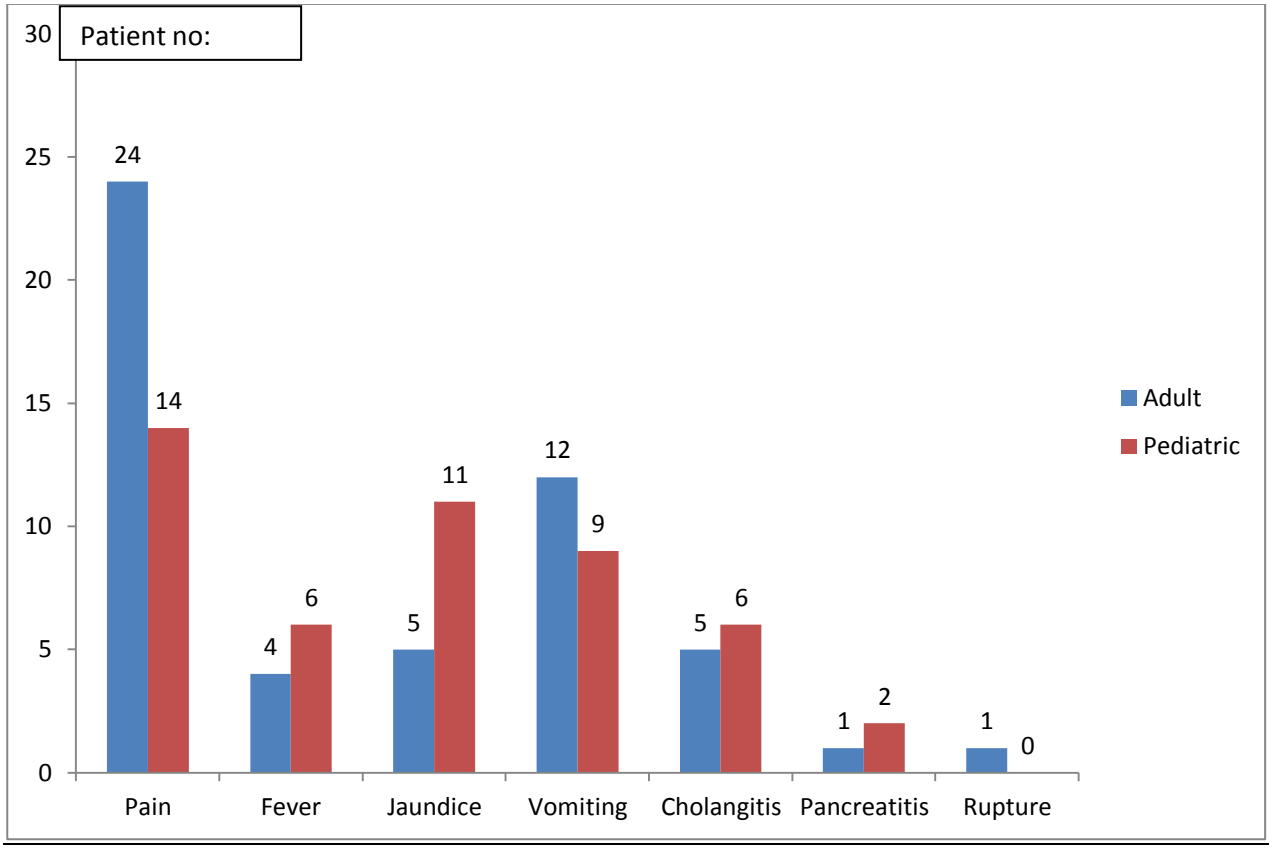
Adult



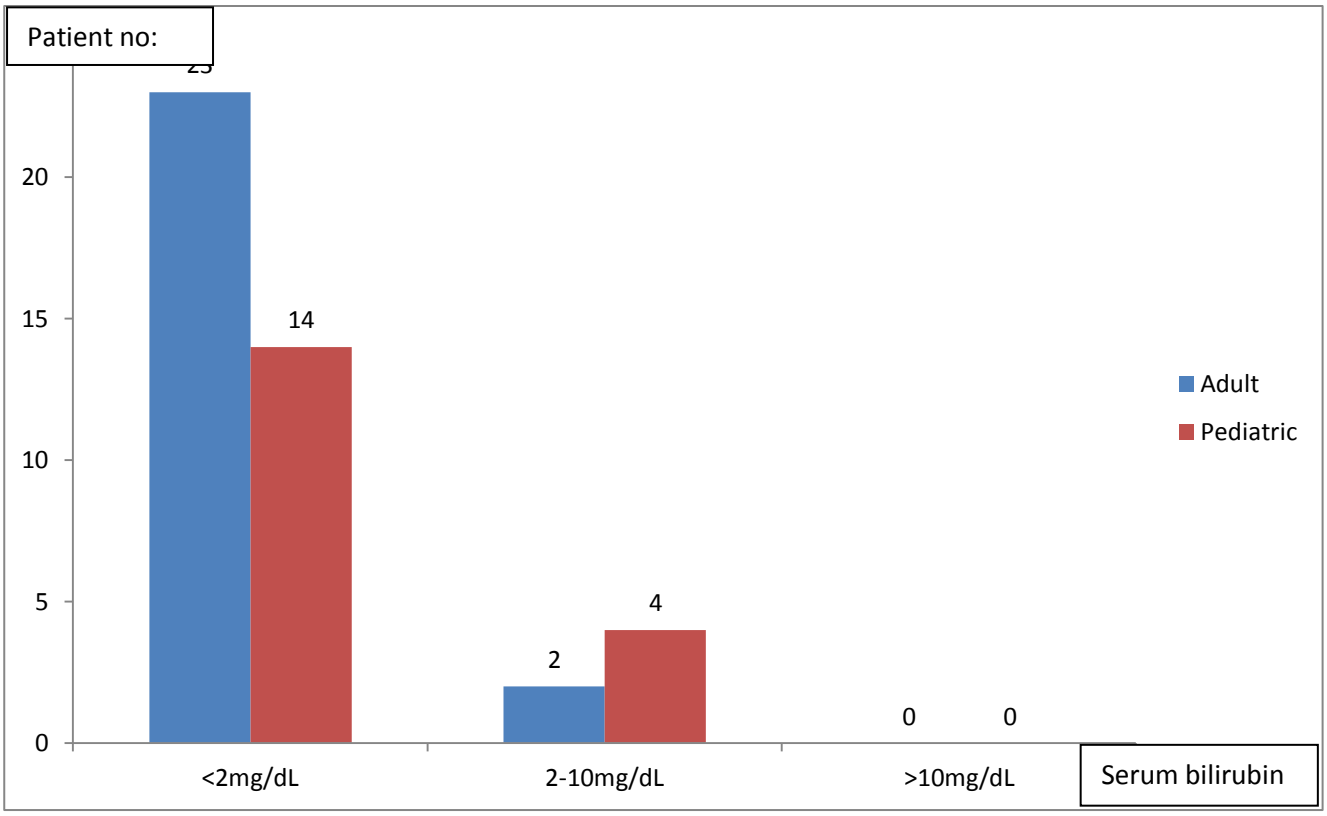
Pediatric



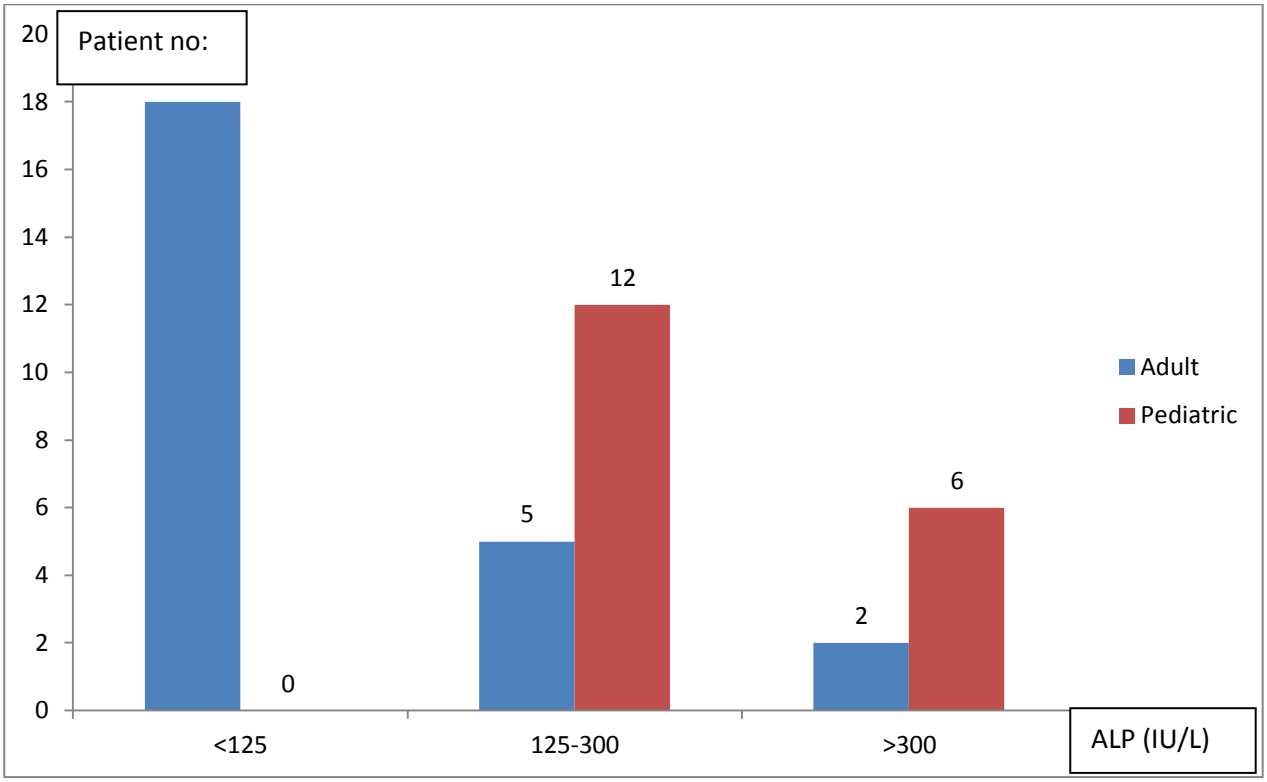
III) Clinical presentation



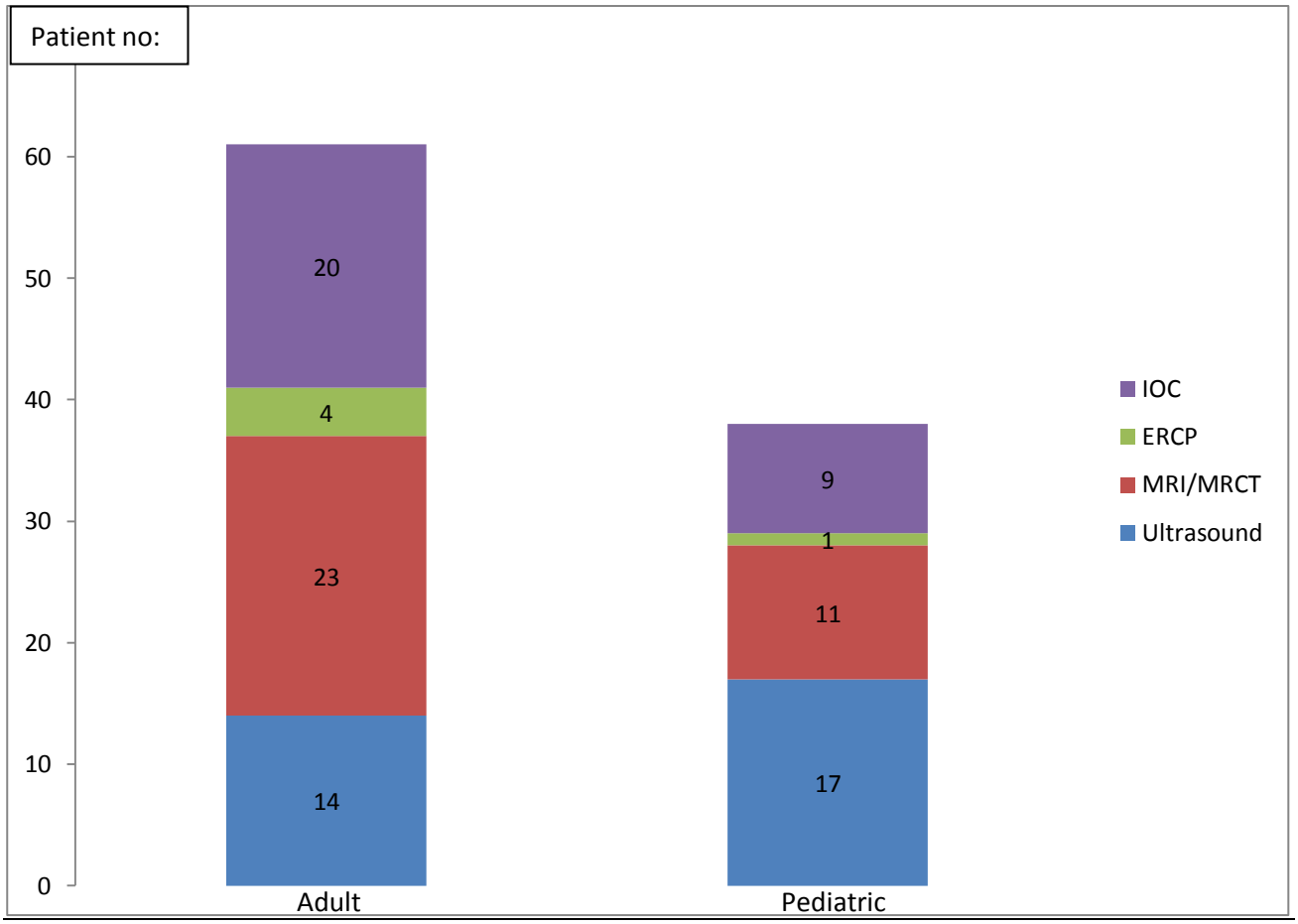
IV) Serum bilirubin



V) Serum alkaline phosphatase

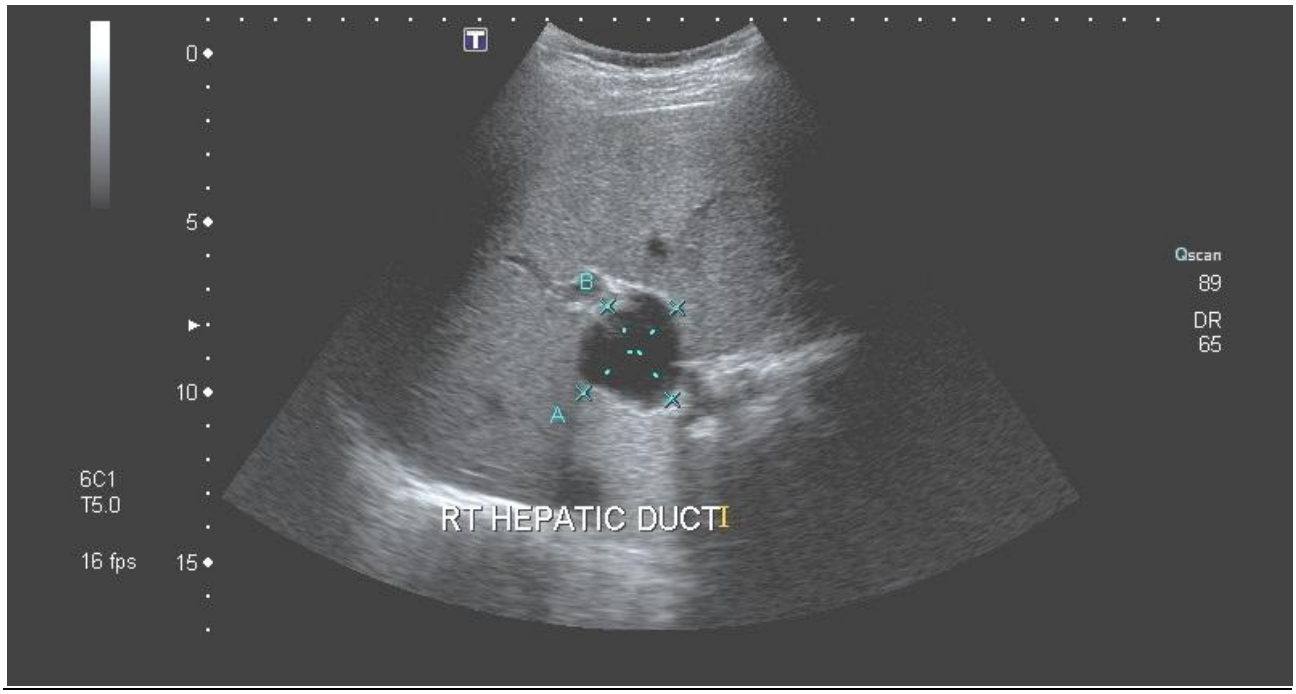


VI) Pre-operative imaging



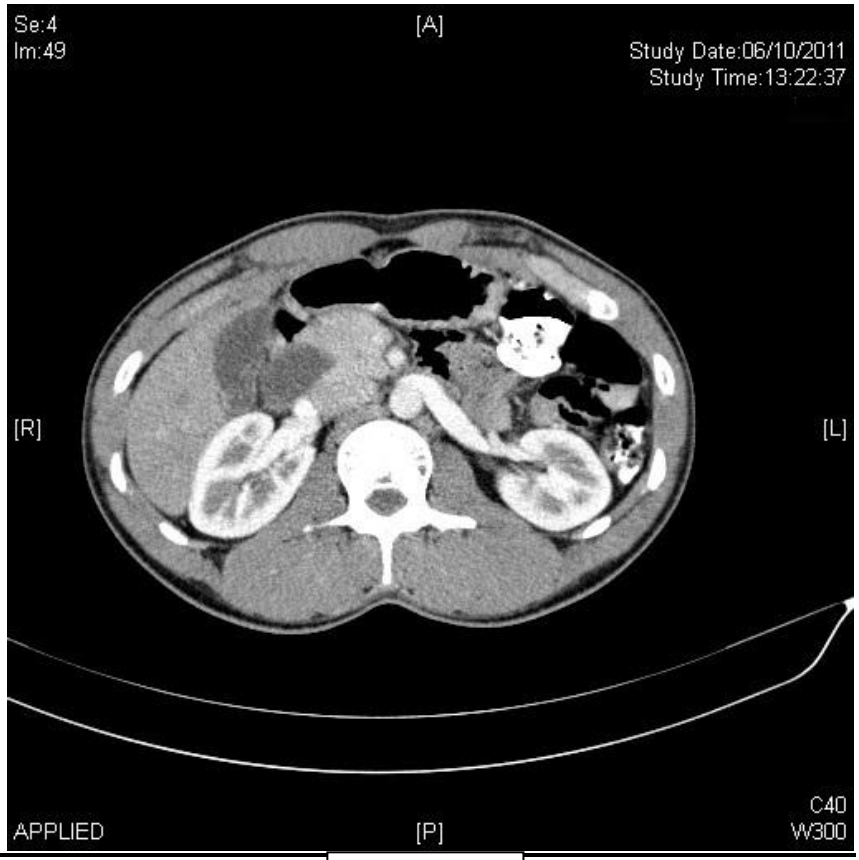
Picture 1 (Ultrasound)

Type IA cyst

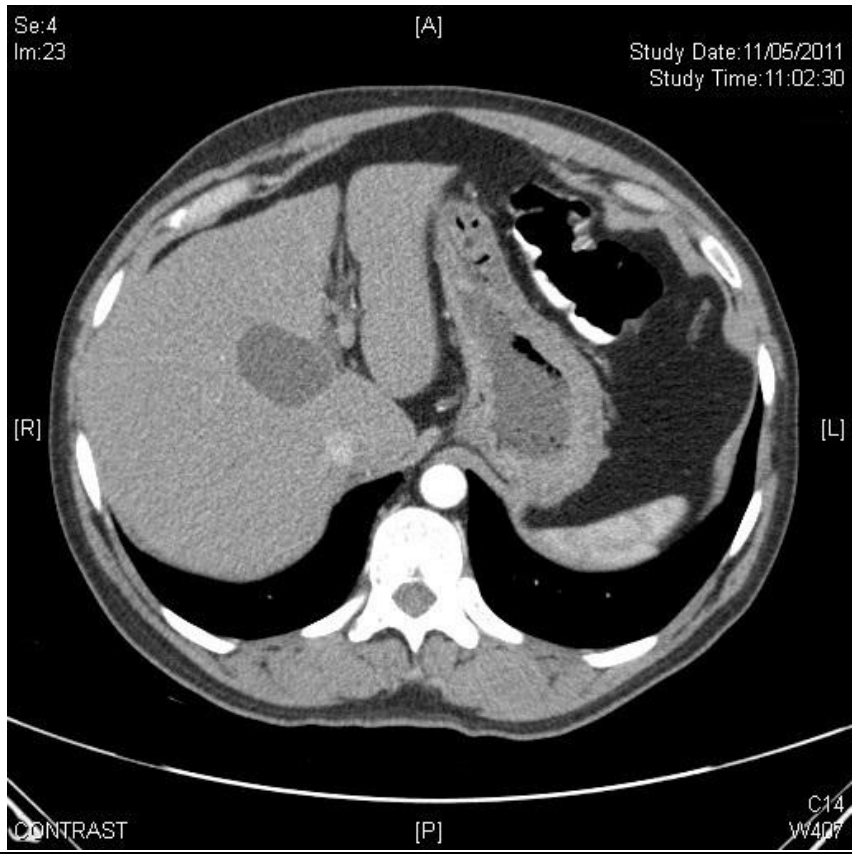


Type IVA cyst with dilated right hepatic duct

Picture 2 (CT)

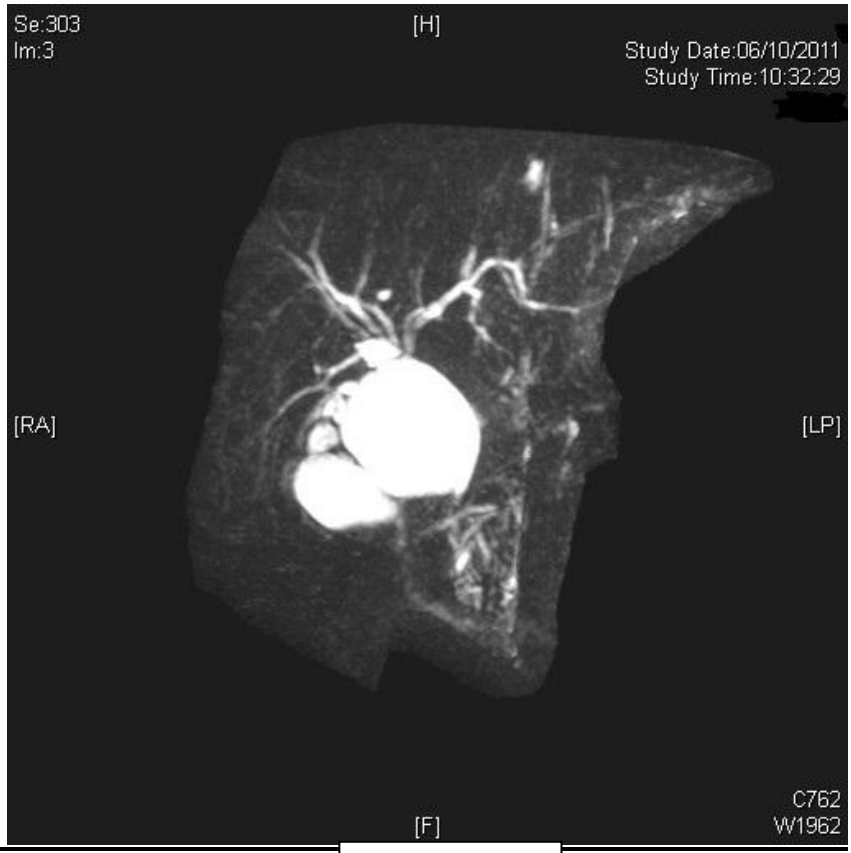


Type IA cyst



Type IVA cyst with dilated right hepatic duct

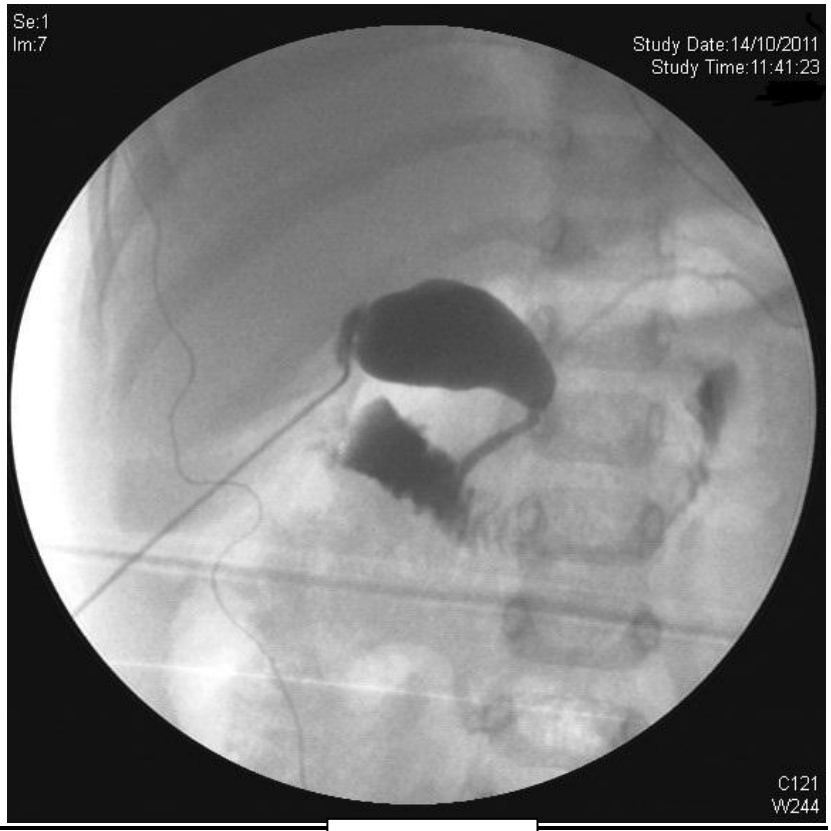
Picture 3 (MRCP)



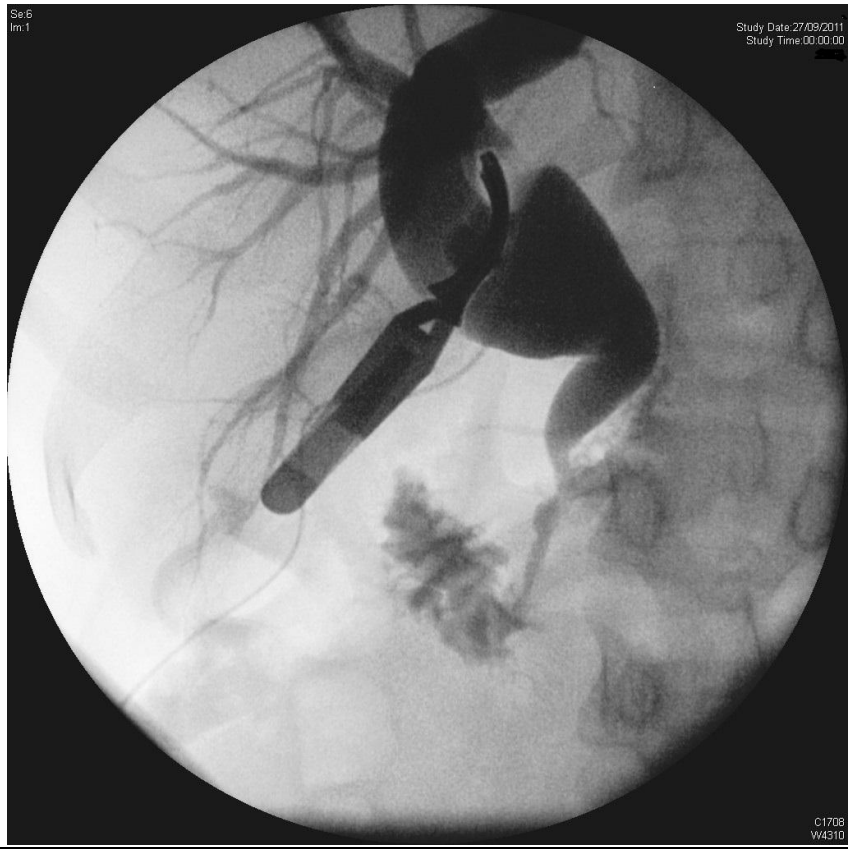
Type IA cyst

Type IVA cyst

Picture 4 (IOC)



Type IA cyst



Type IVA cyst

Picture 5 (ERCP)

Type IA cyst with choledocholithiasis

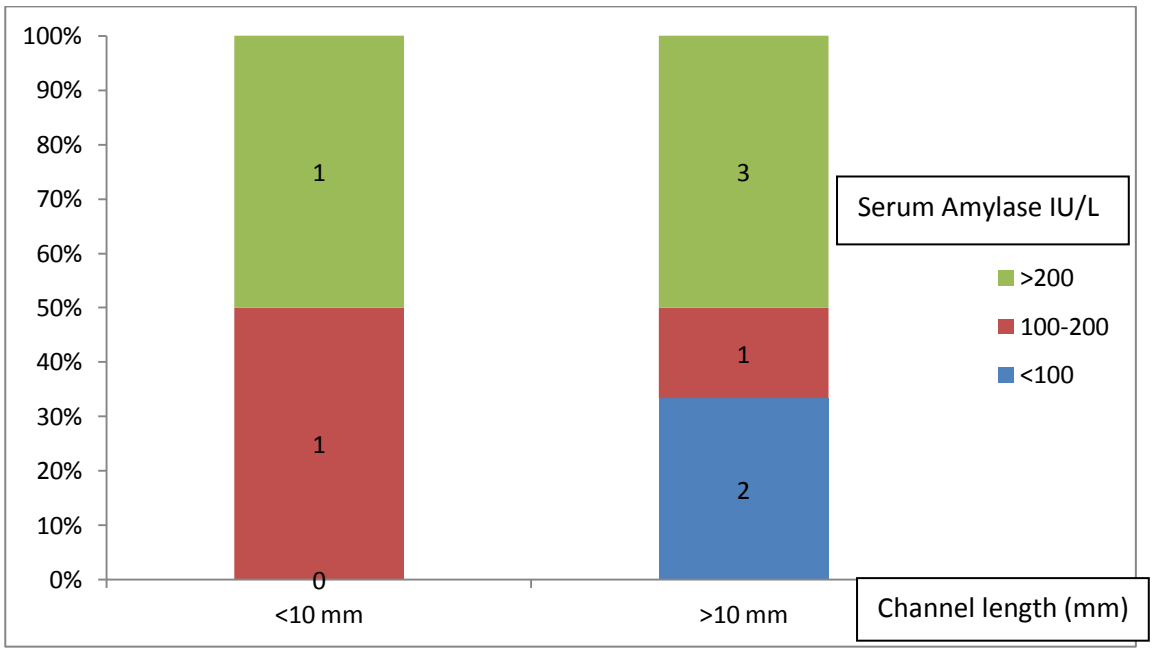
Type IVA cyst with choledocholithiasis

Picture 6 (T-tube cholangiogram)

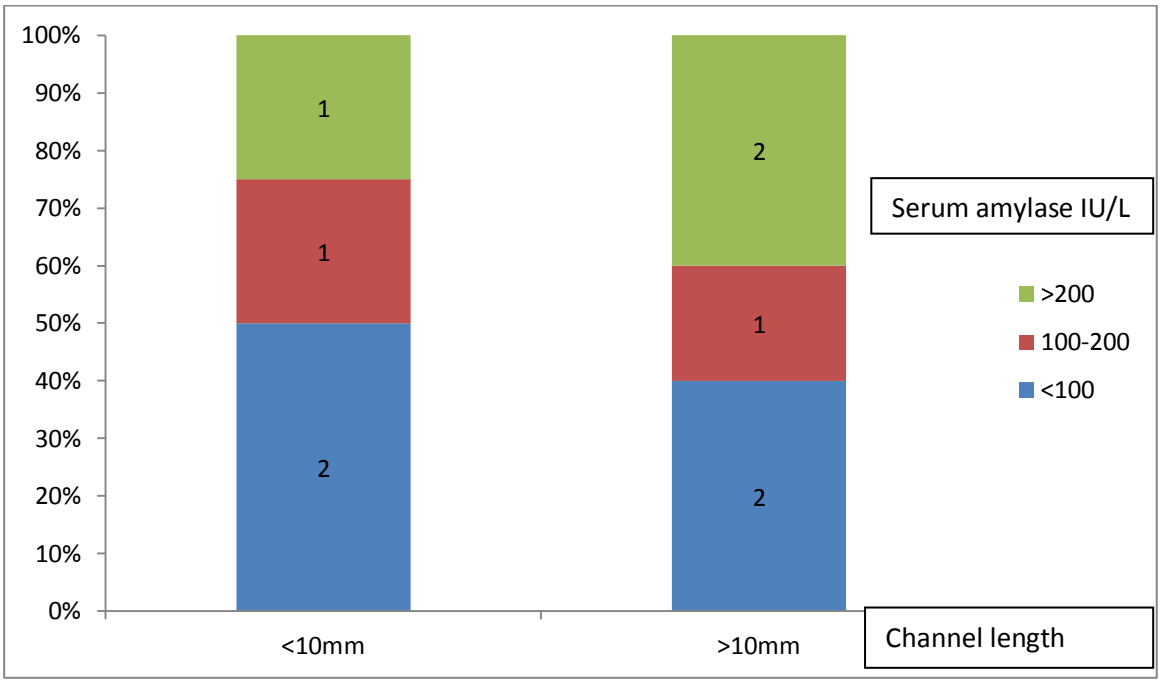
Type IA cyst

VII) Serum amylase vs. channel length

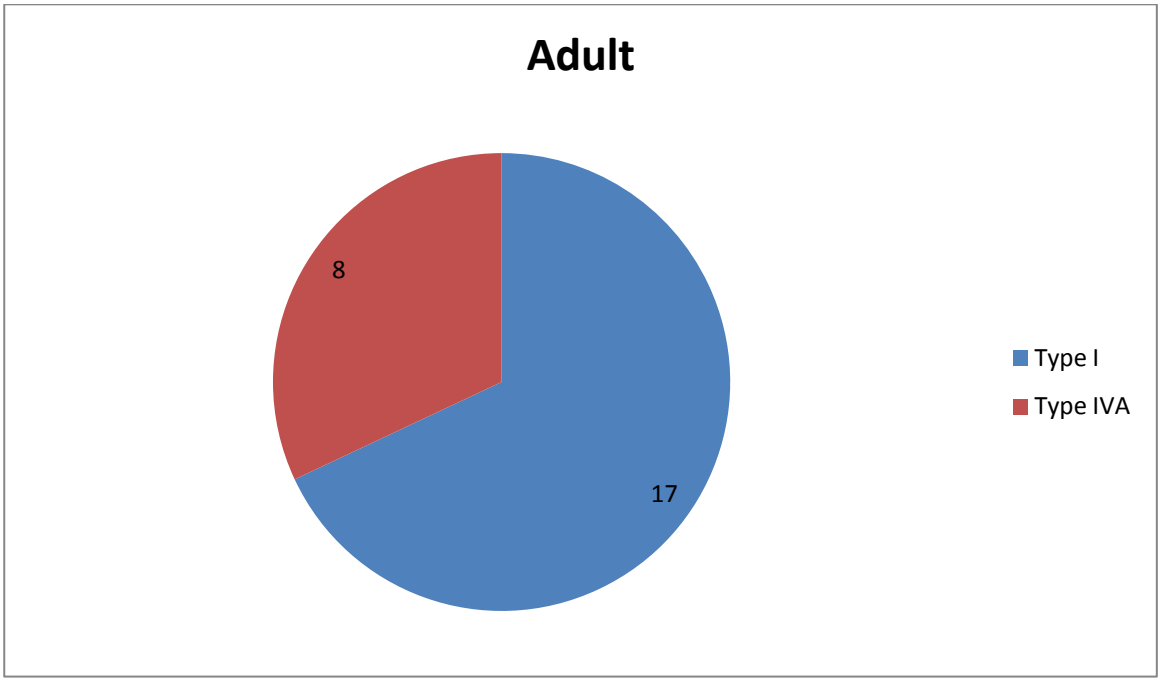
Adult

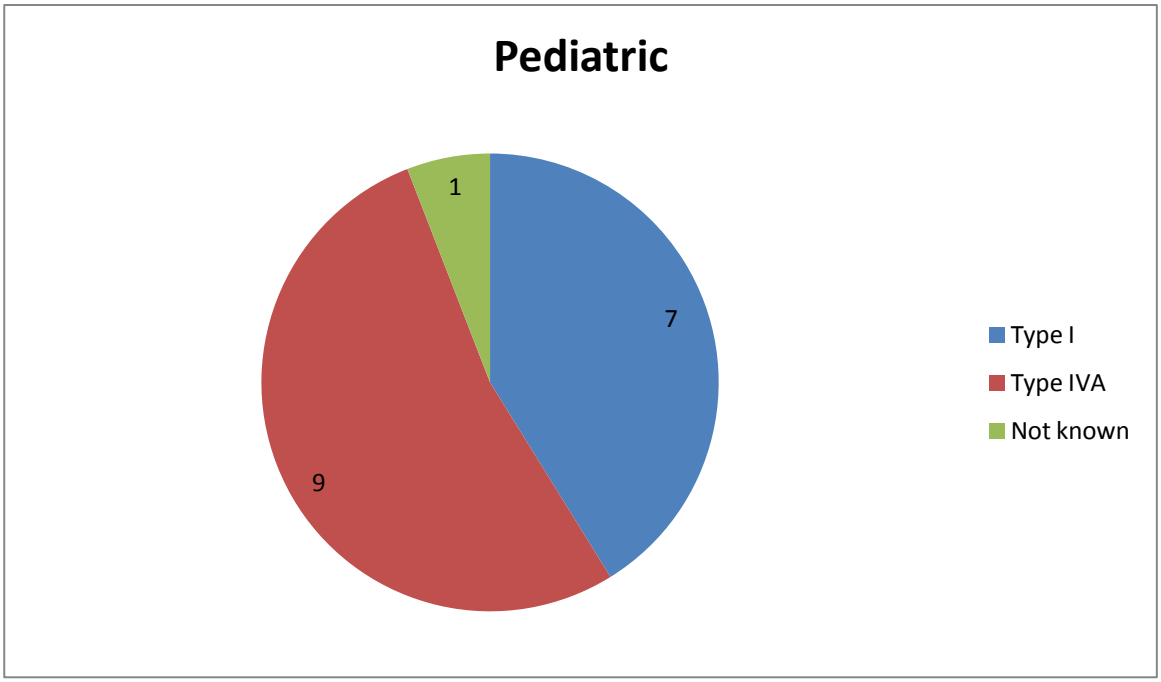


Pediatric

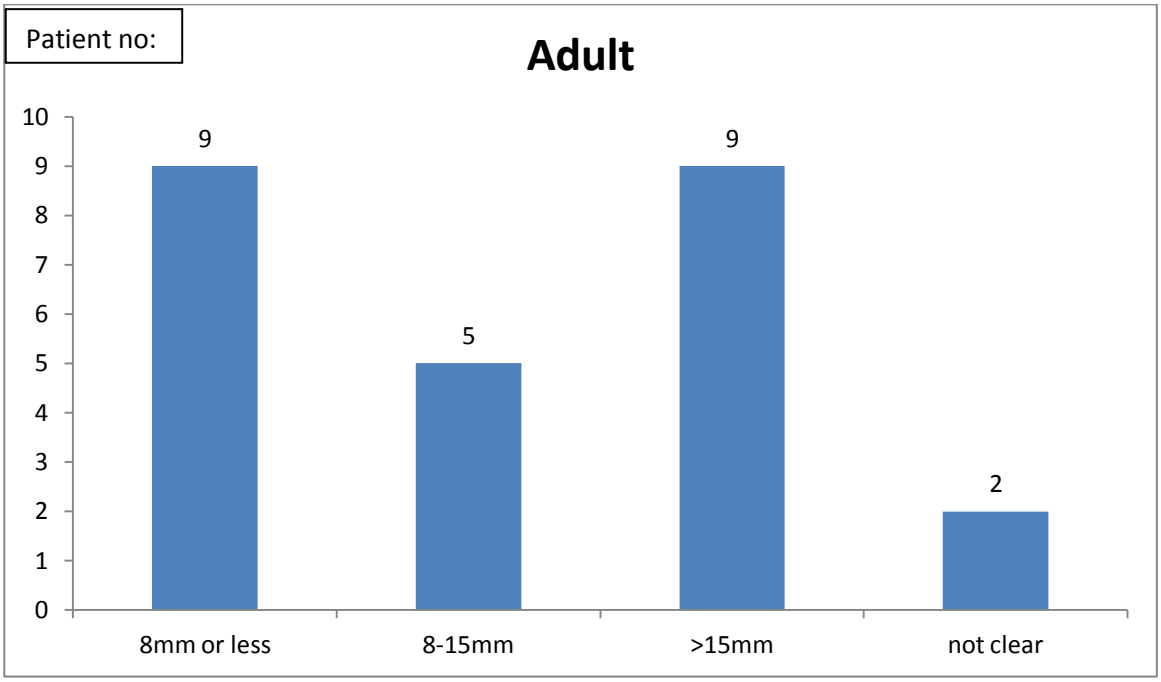


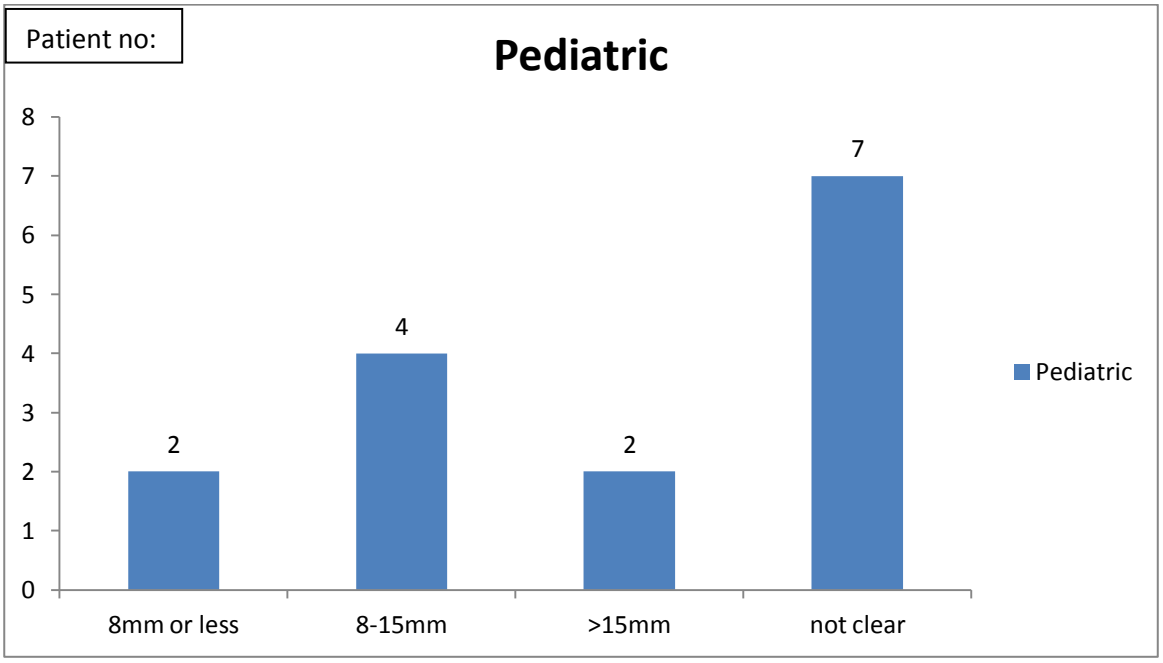
VIII) Cyst type



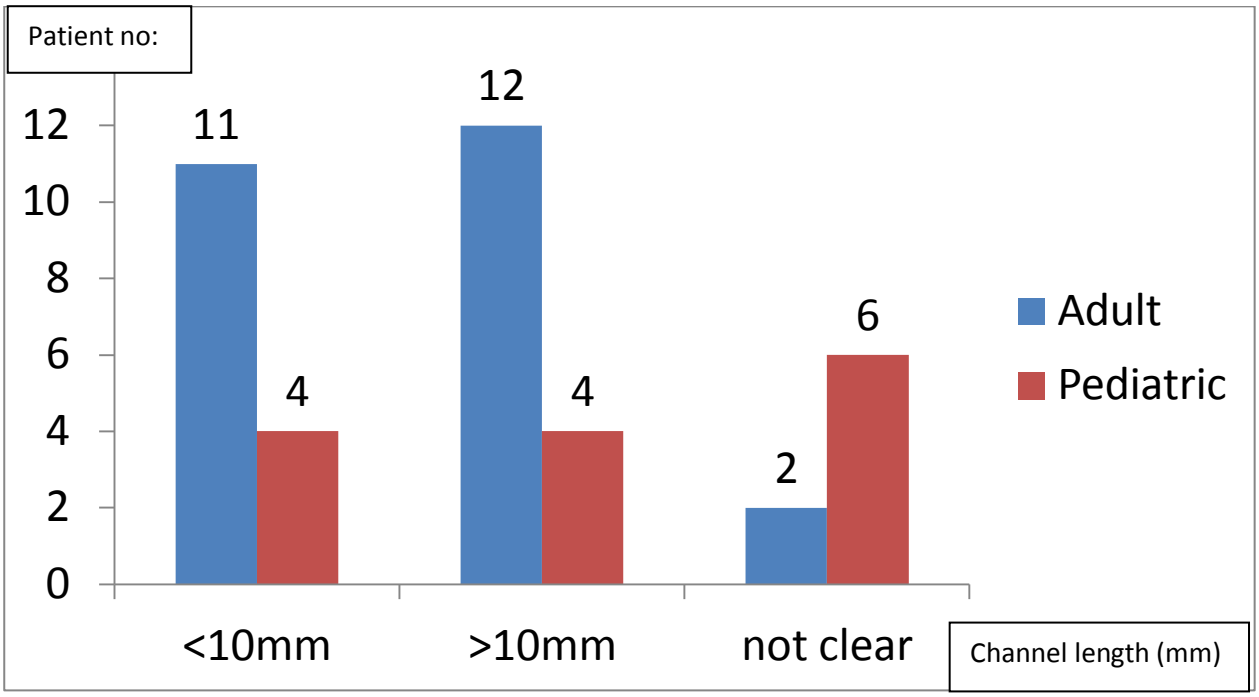


IX) Pancreatico-biliary junction length



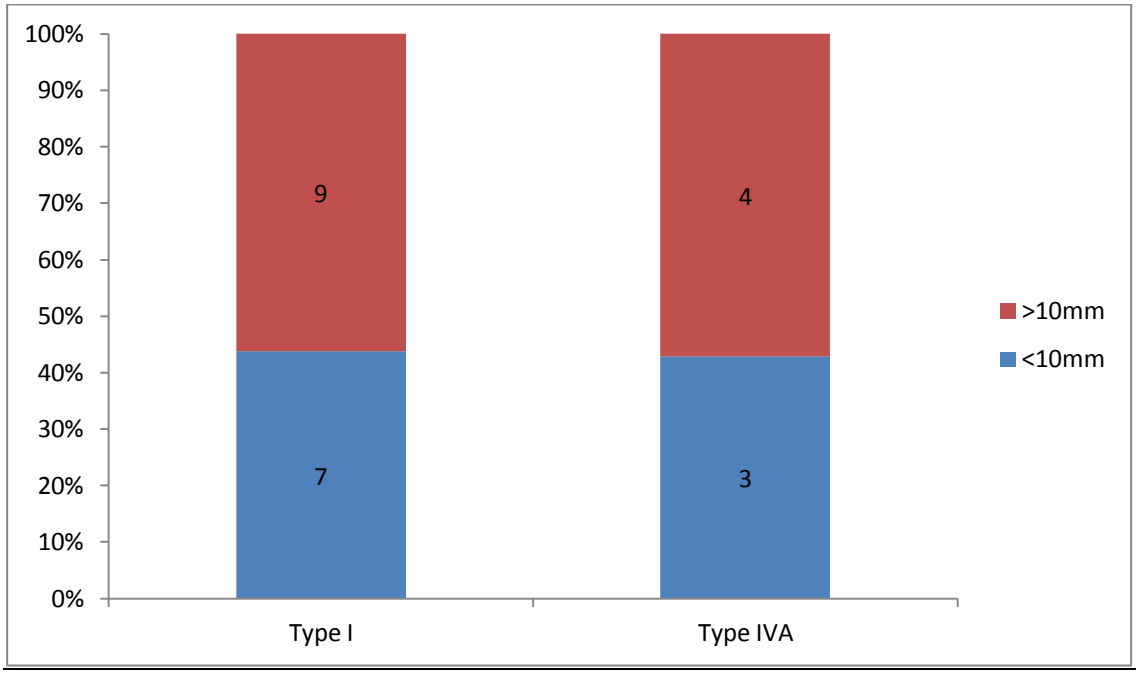


X) Long common channel



XI) Cyst type vs. junction length

Adult



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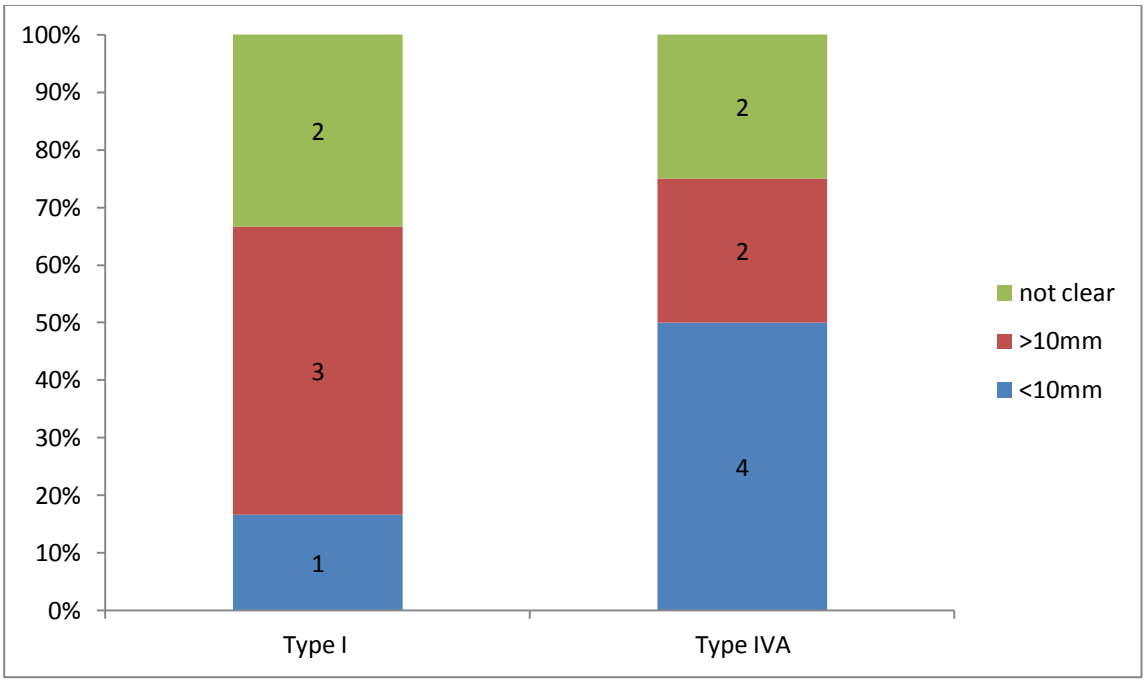
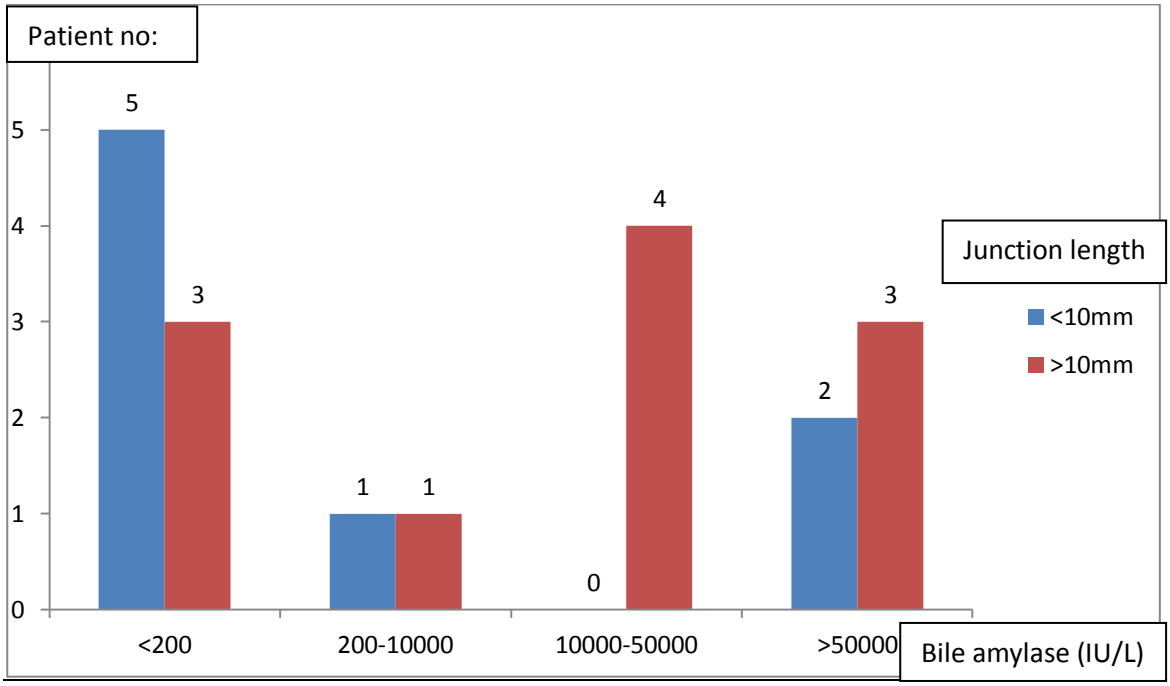


XII) Junction length vs. bile amylase level

Adult



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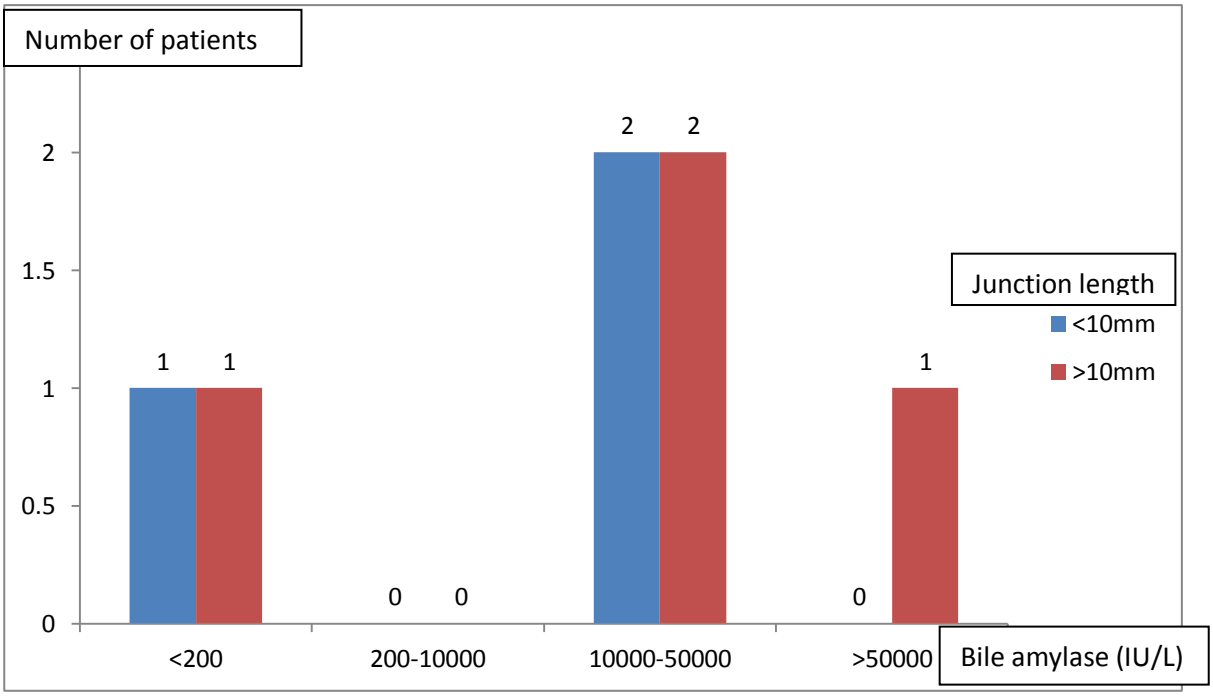
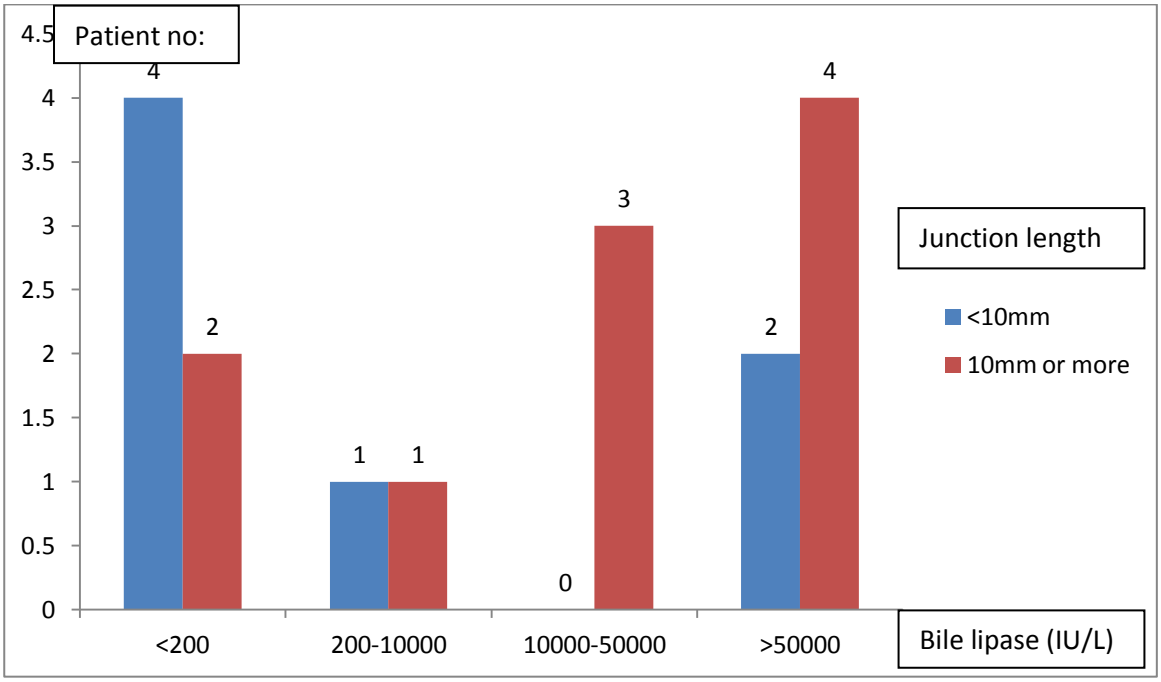
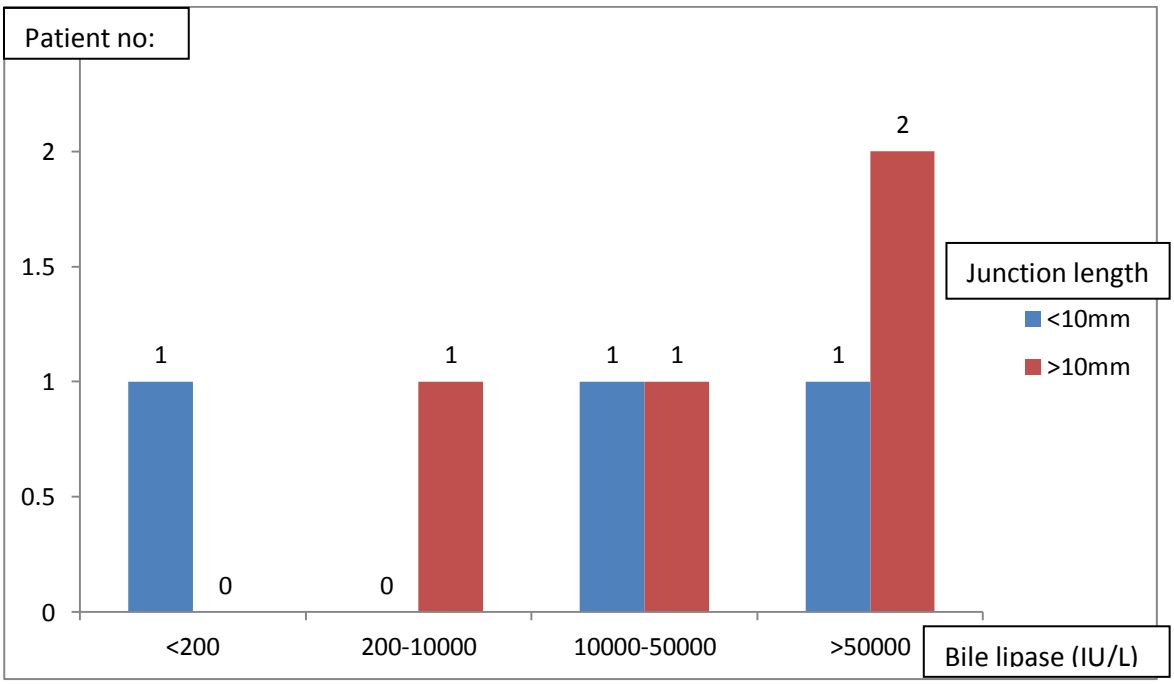


XIII) Junction length vs. bile lipase

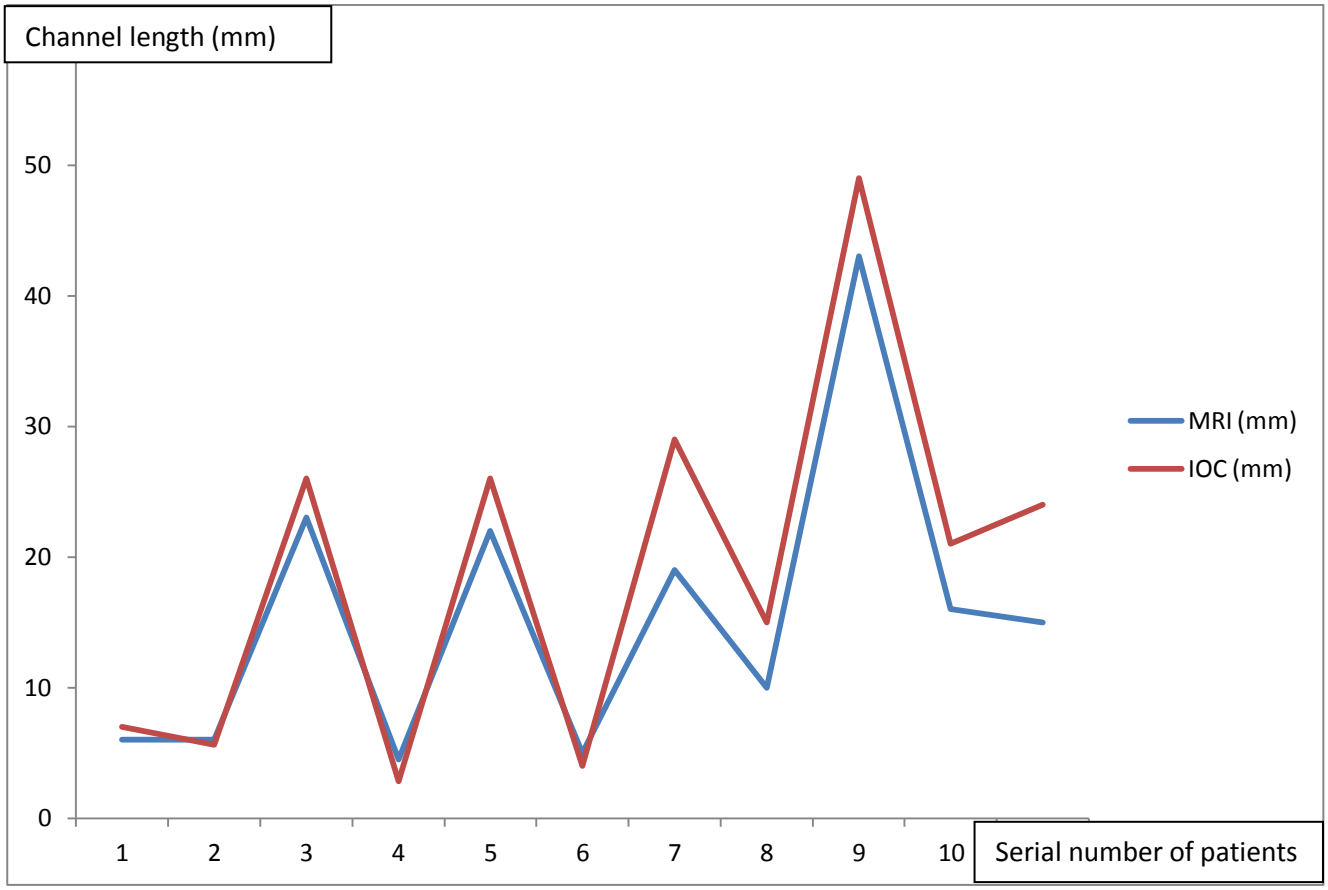
Adult



Pediatric

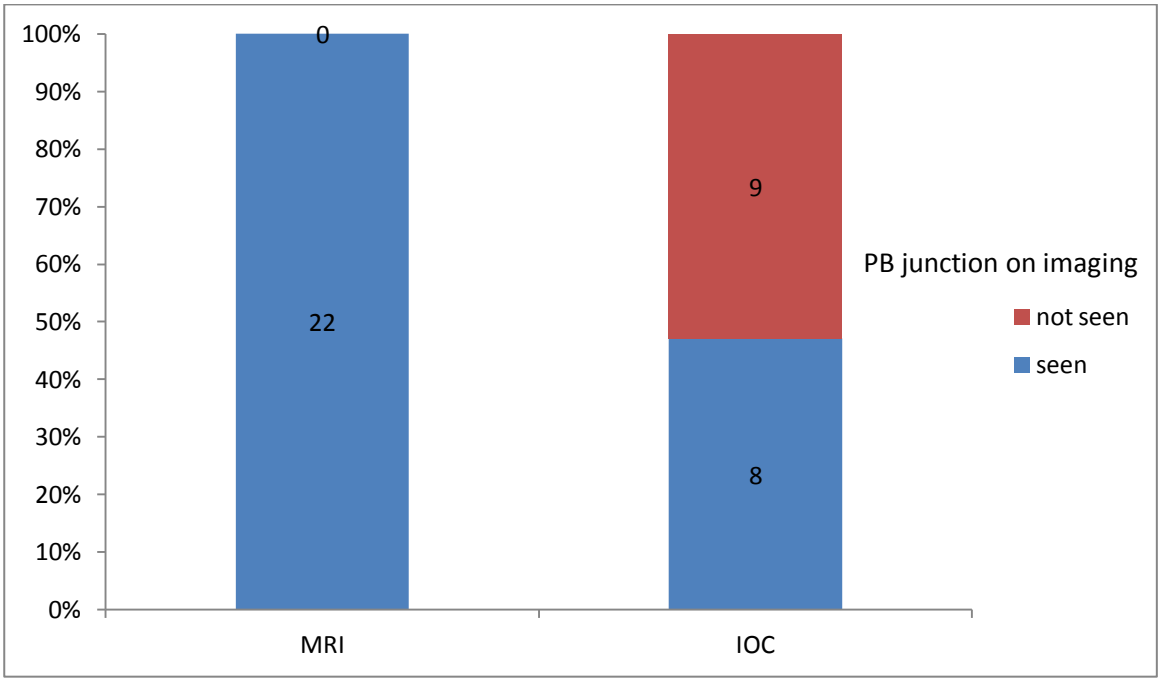


XIV) Comparison of MRCP with Intra-operative cholangiogram (IOC)

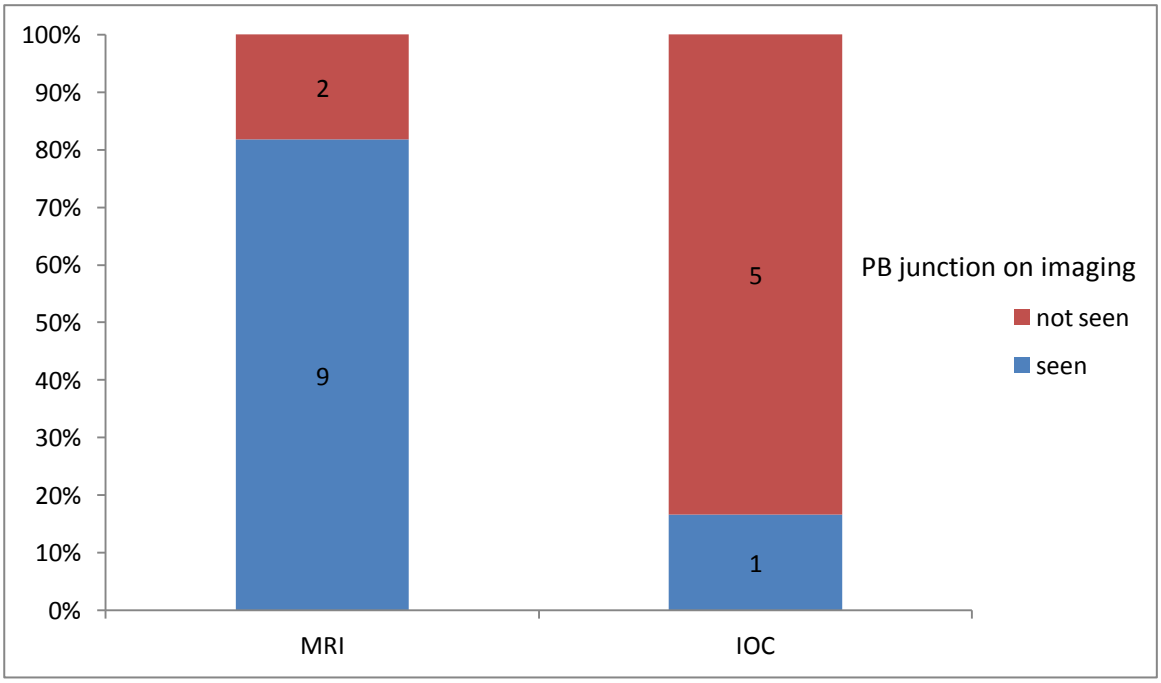


XV) Junction identification on MRI and IOC

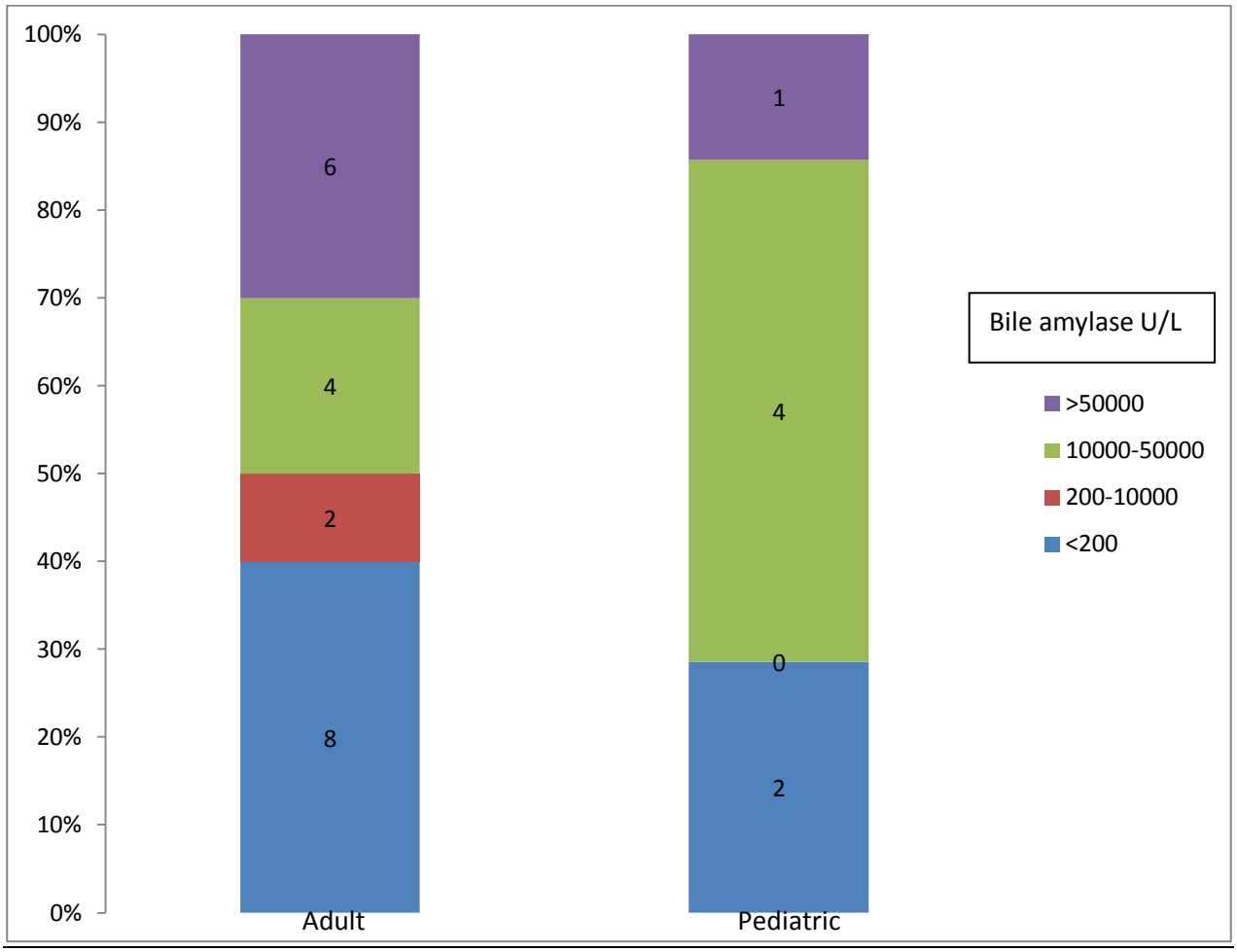
Adult



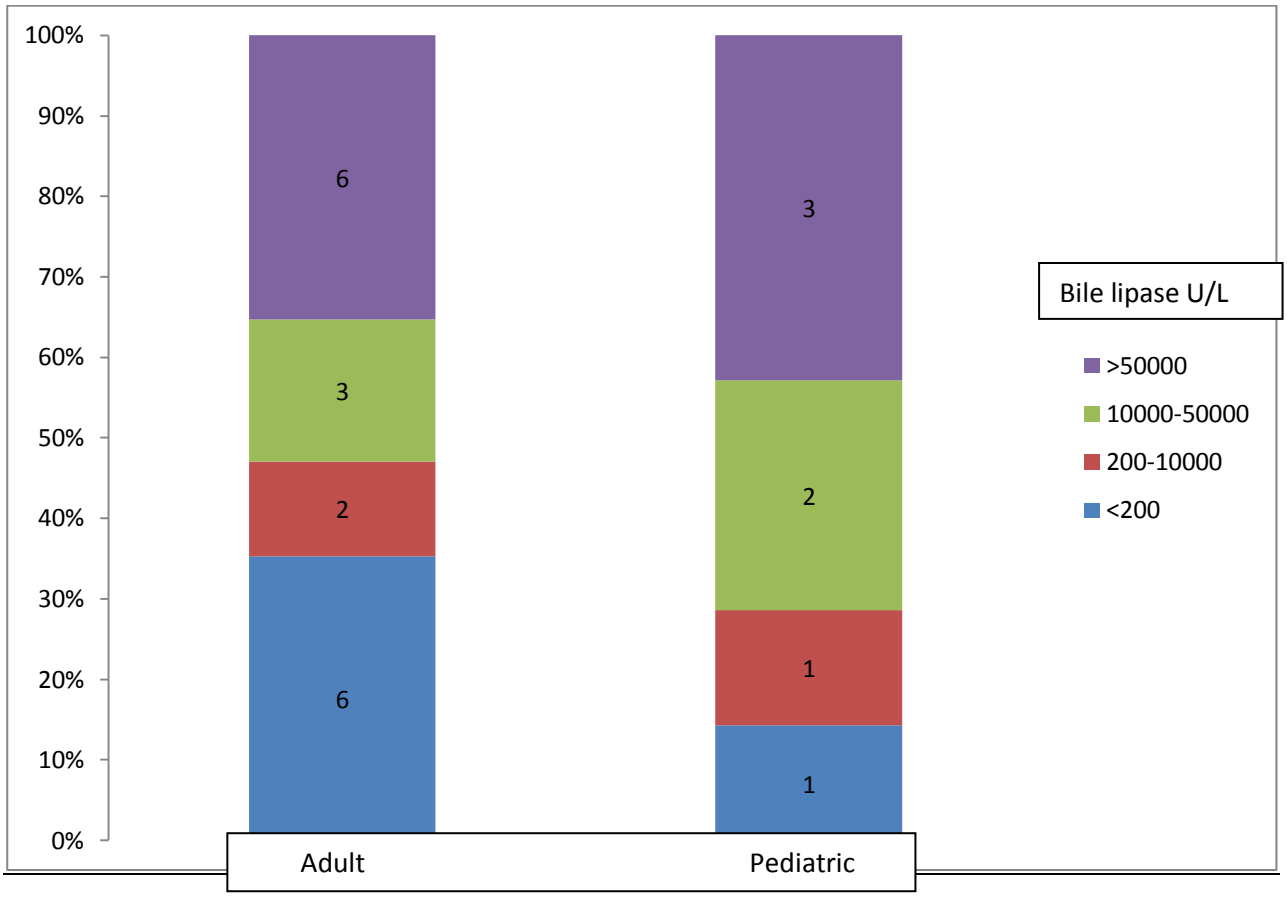
Pediatric



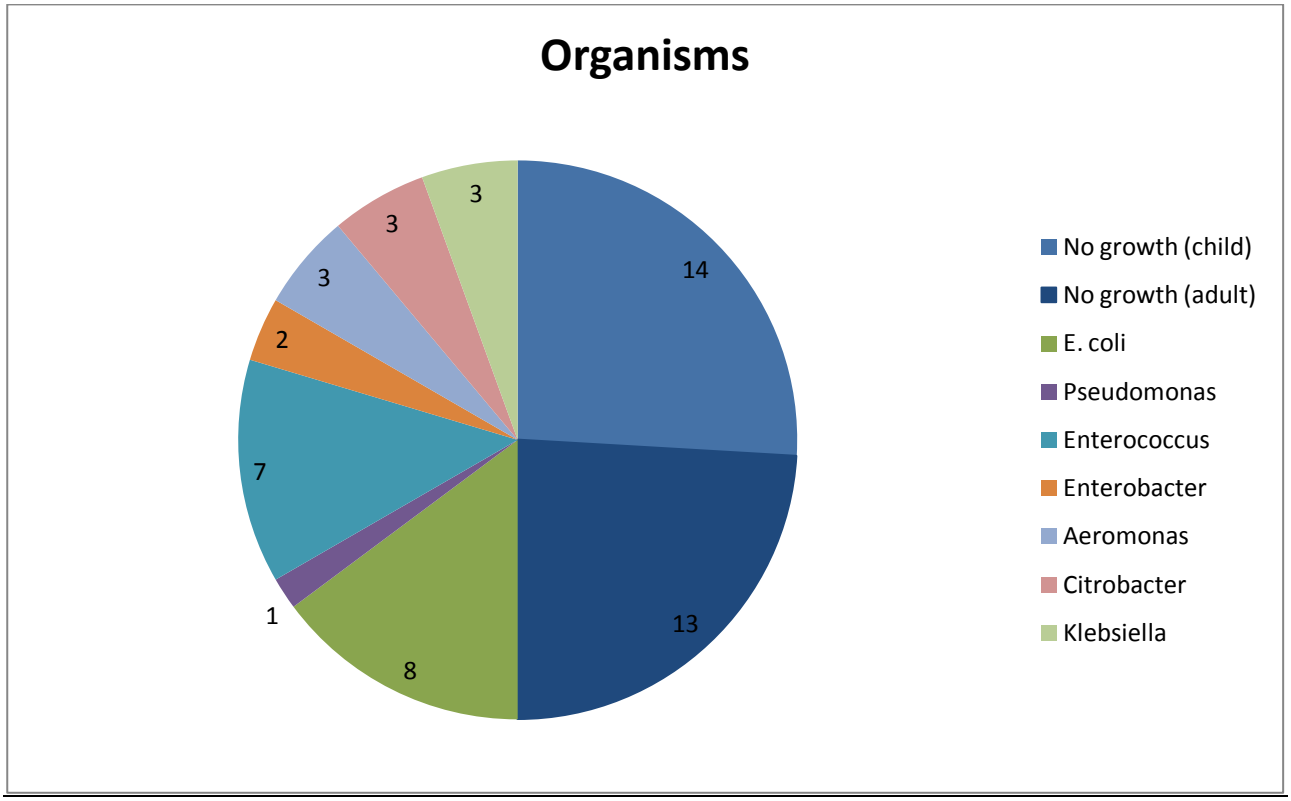
XVI) Bile amylase level vs. age



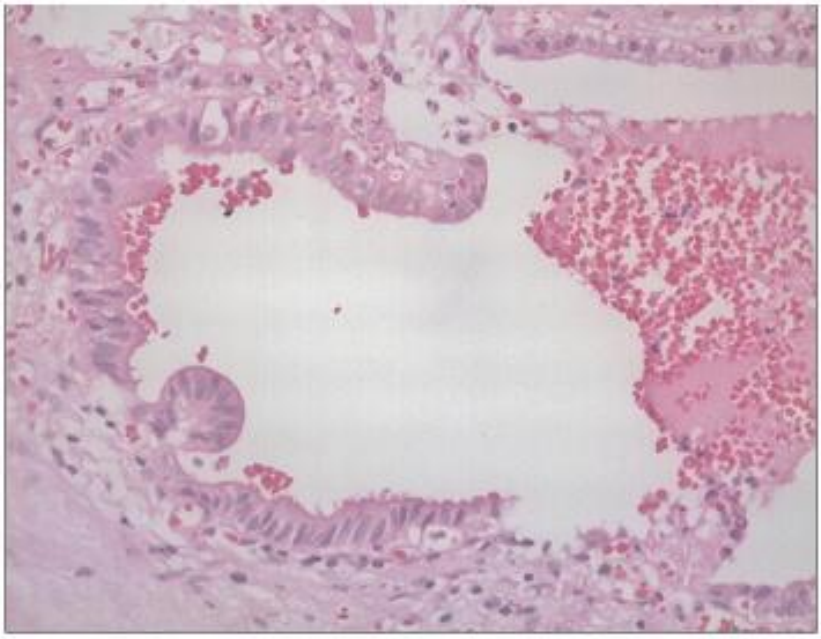
XVII) Bile lipase level vs. age



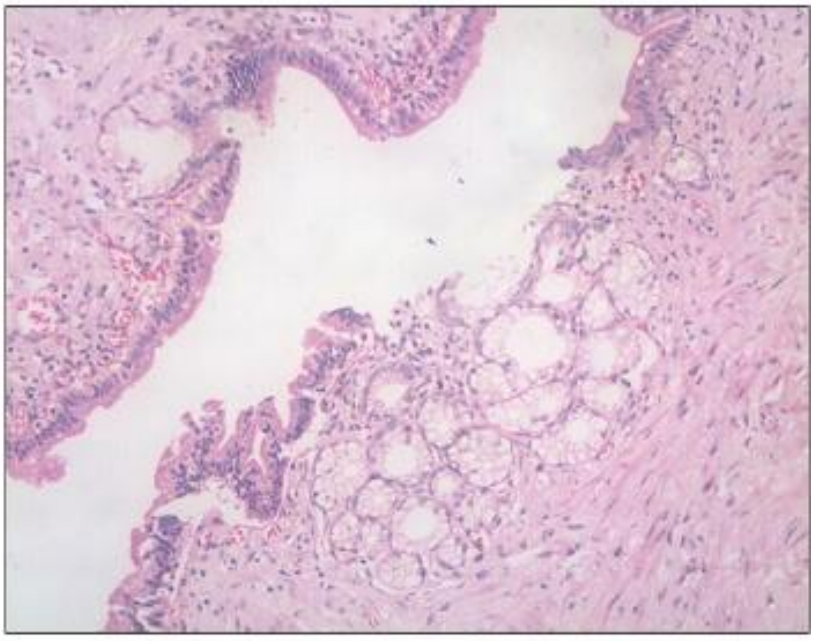
XVIII) Bile culture in adults and children



Picture 7 (Epithelial hyperplasia, metaplasia)

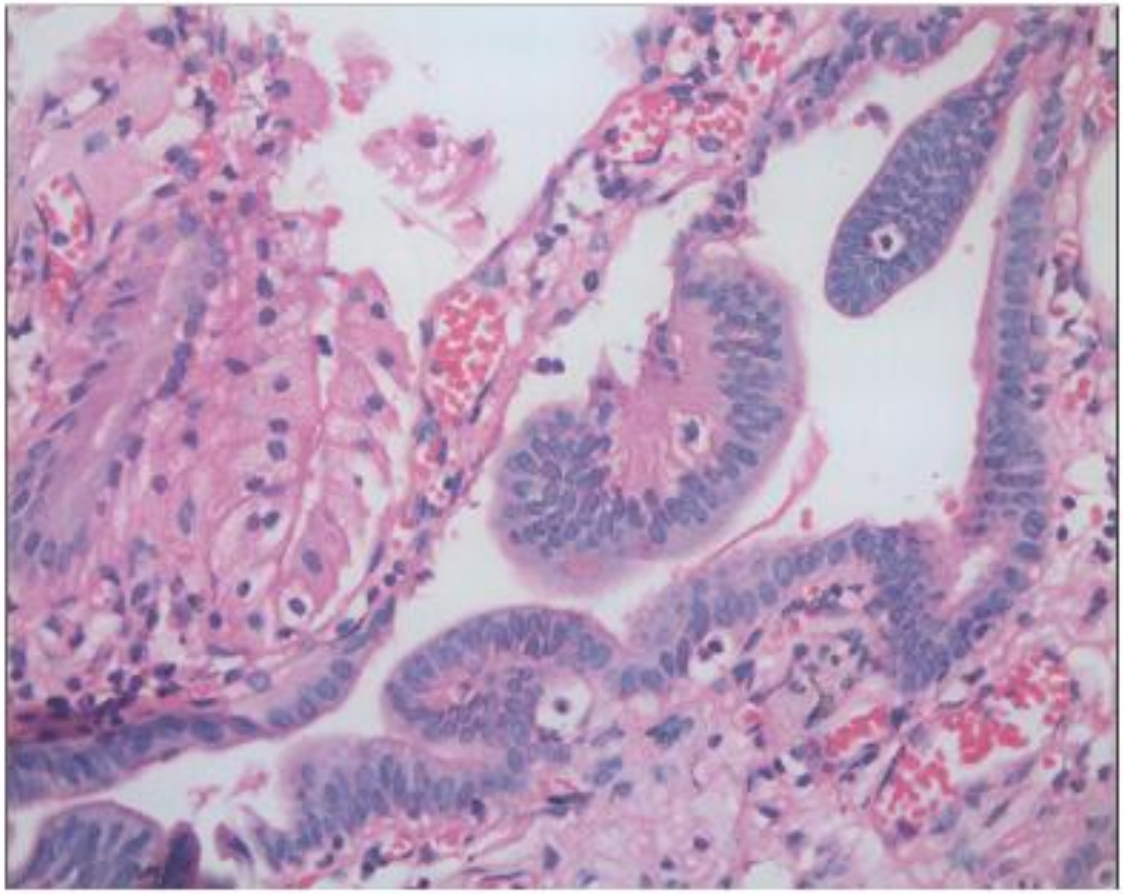


Micropapillary hyperplasia

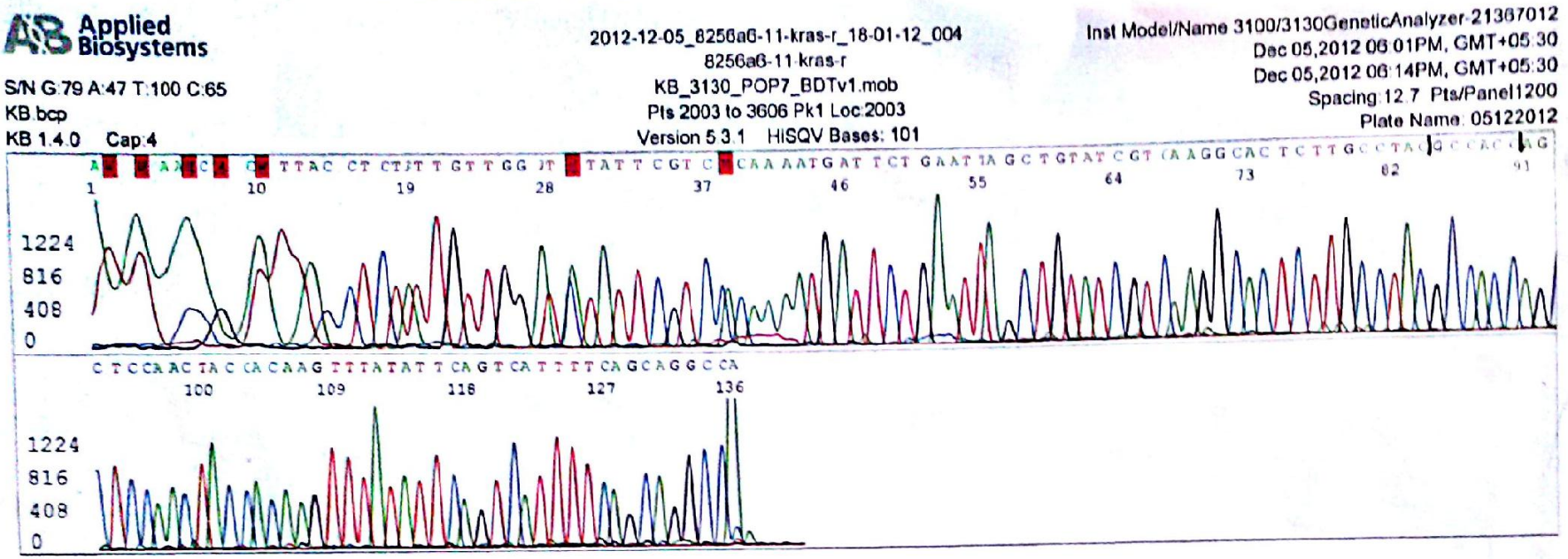


Pyloric gland metaplasia

Picture 8 (Biliary Intraepithelial Neoplasia- BilIN)

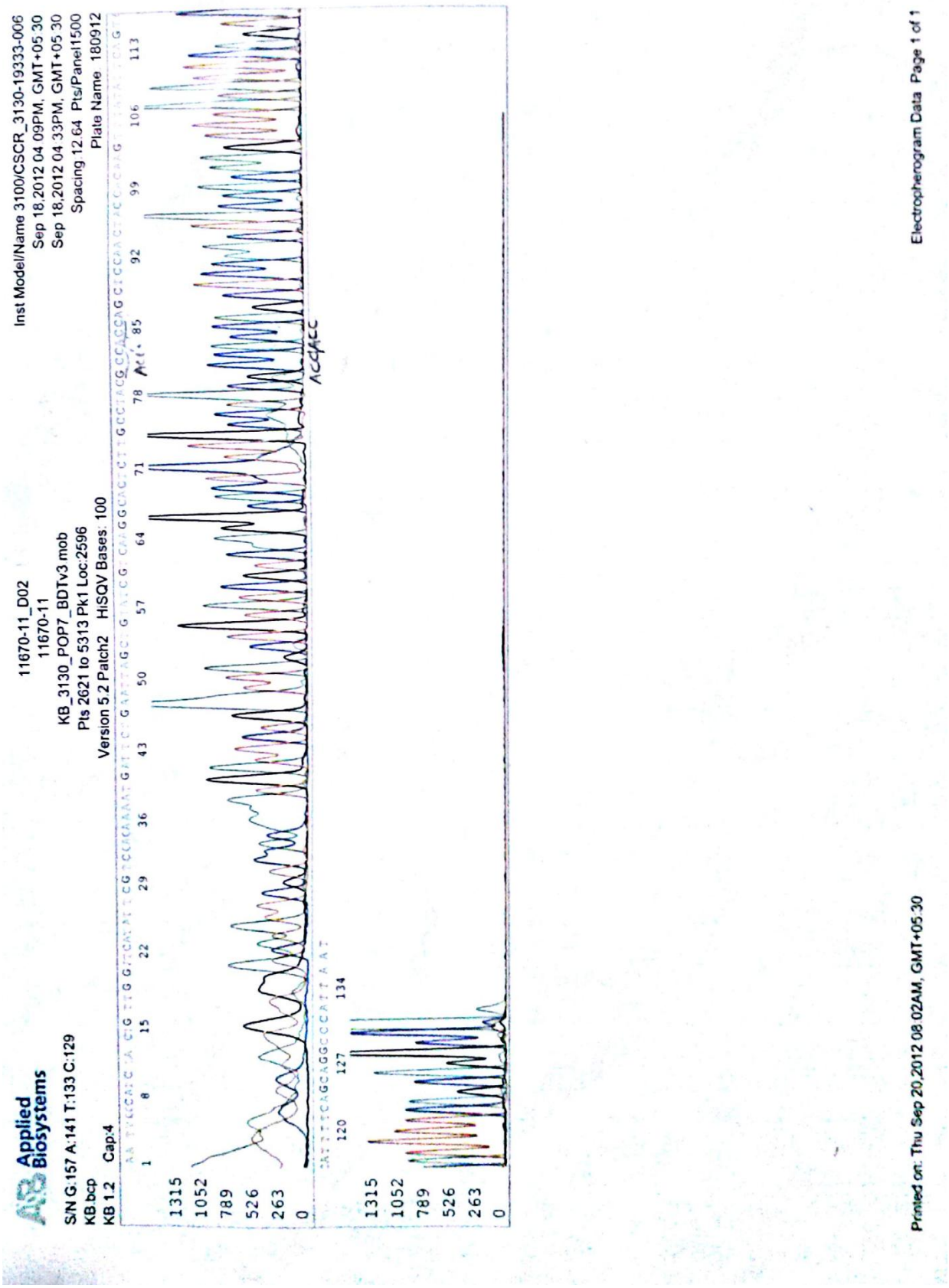


Biliary Intra-epithelial Neoplasia

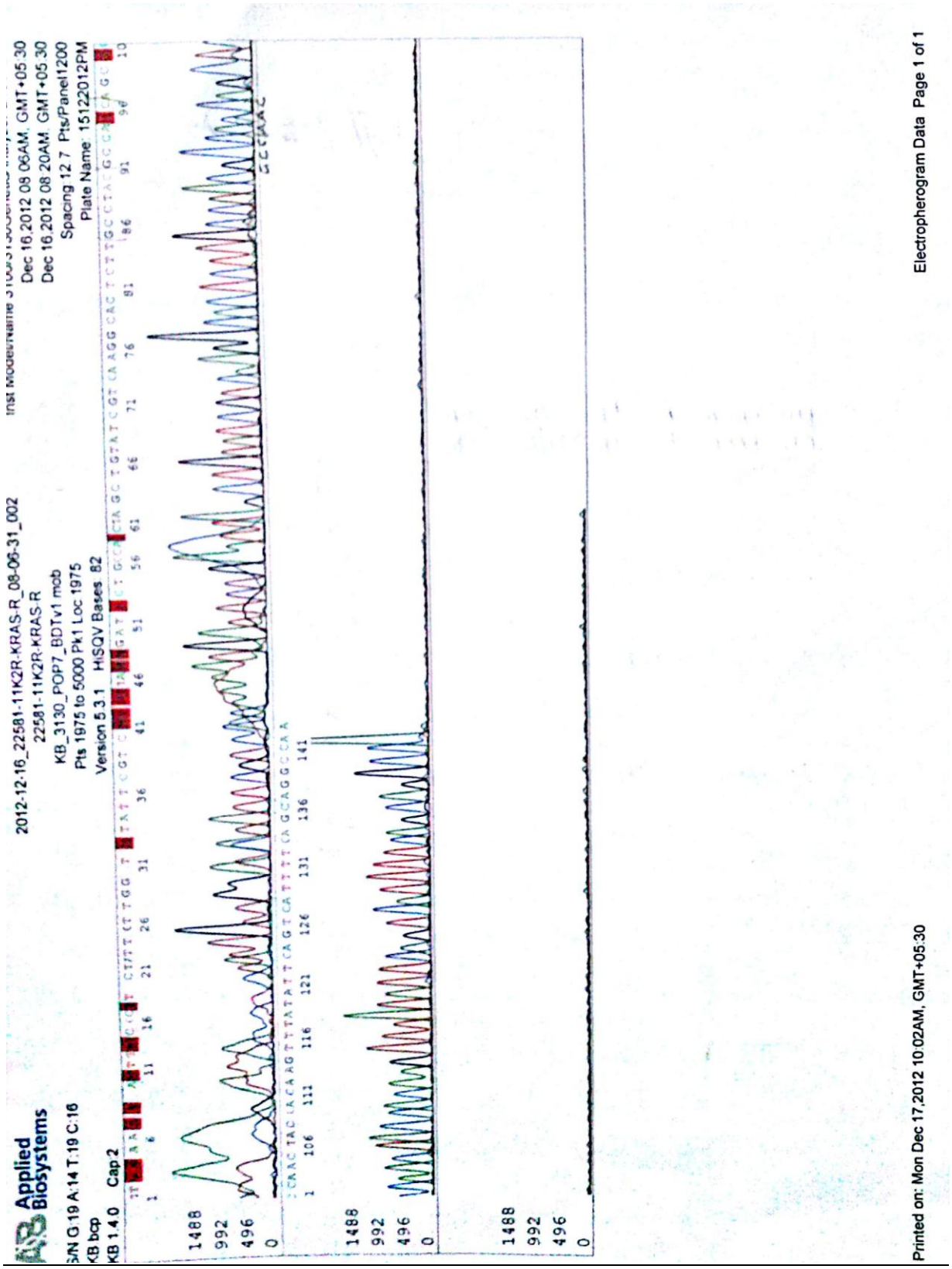


Picture 9 (K-ras normal reverse sequence)

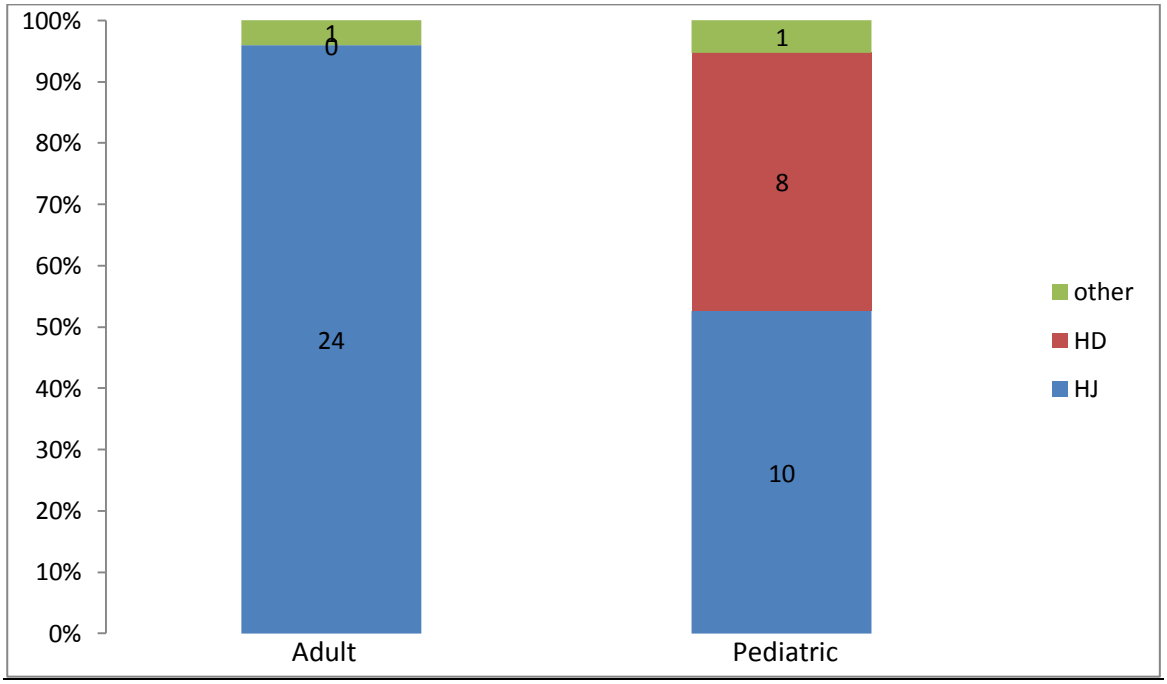
Picture 10 (K-ras reverse sequence: codon 13 GCC to ACC mutation)



Picture 11 (K-ras reverse sequence: codon 12 ACC to AAC mutation)



Operation performed (chart XIX)



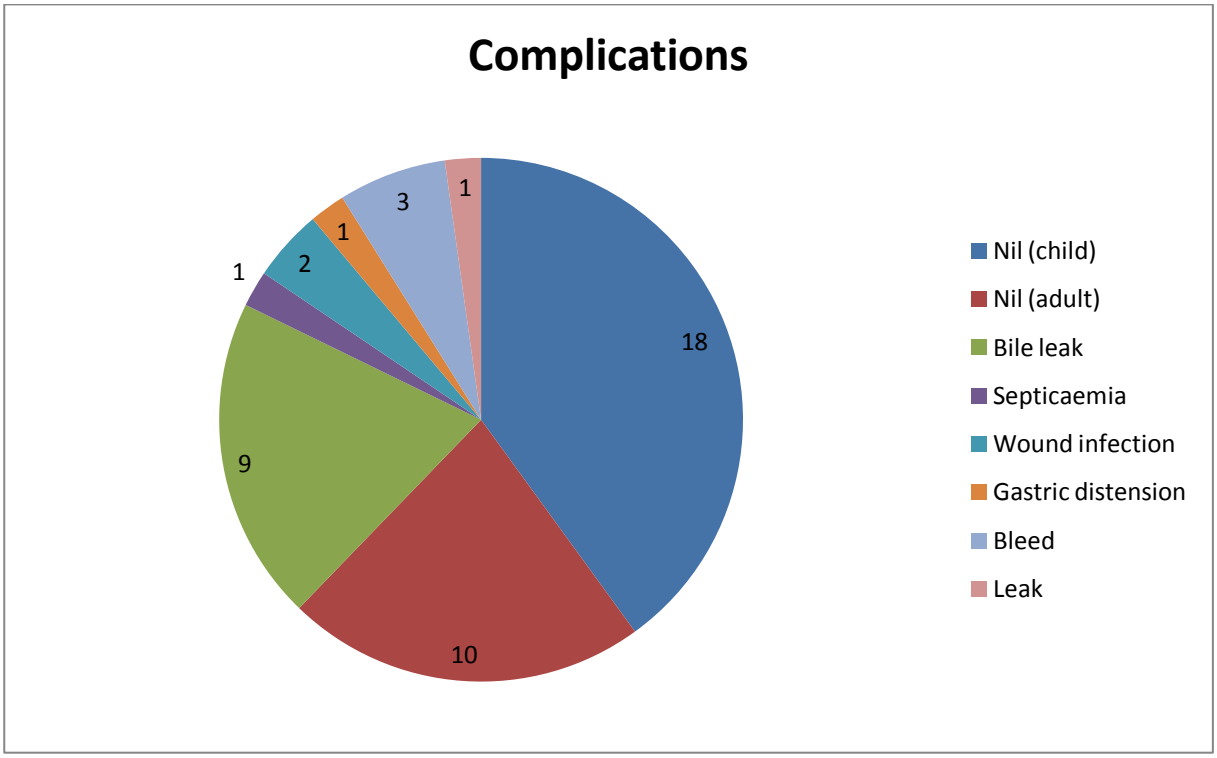
HD: end to side Hepatico-duodenostomy (open)

HJ: end to side Hepatico-jejunostomy (open)

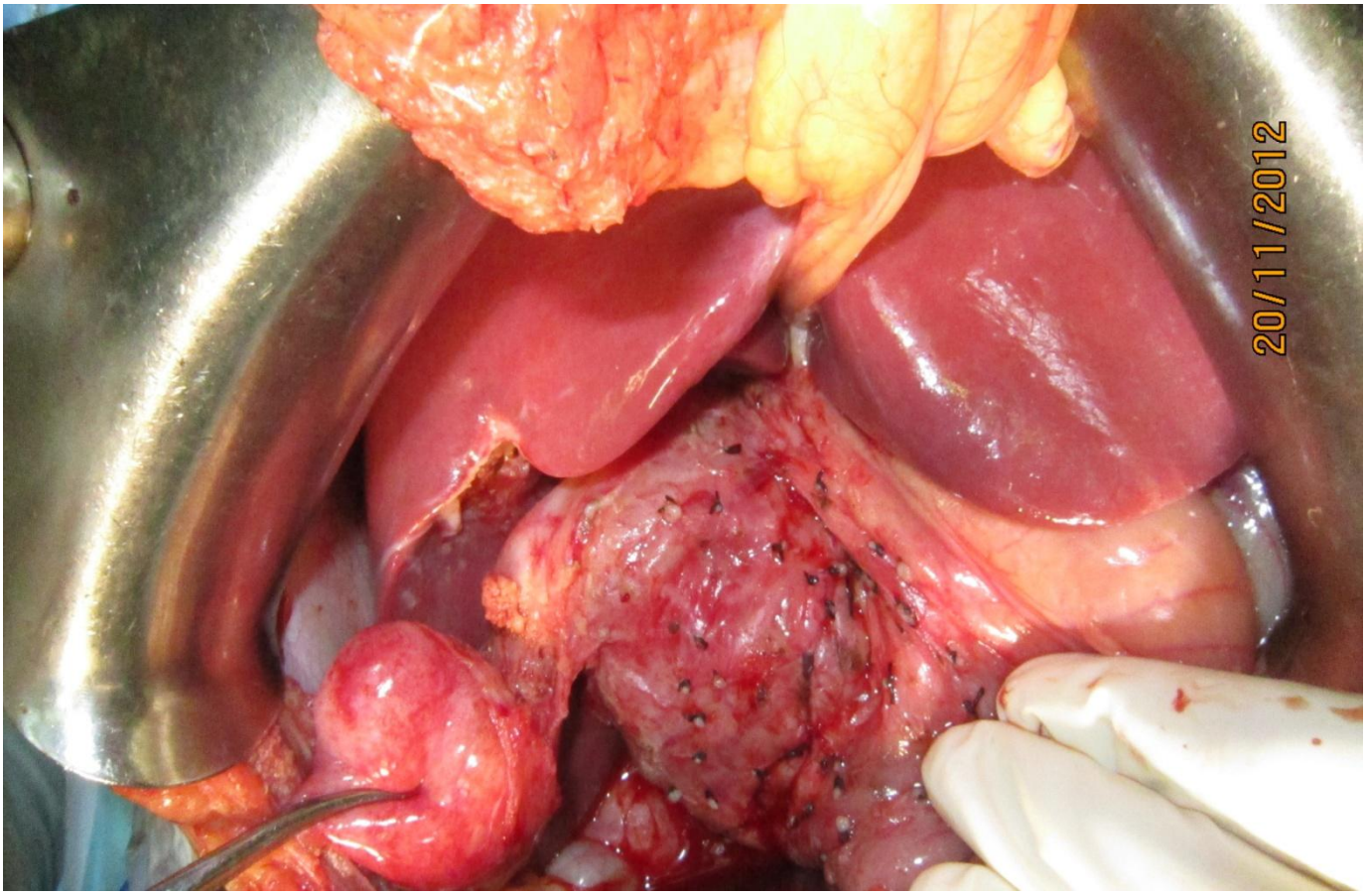
Other: Laparoscopic hepatico-duodenostomy (pediatric) - 1

Radical cholecystectomy + hepatico-jejunostomy (adult) – 1

Complications (chart XX)

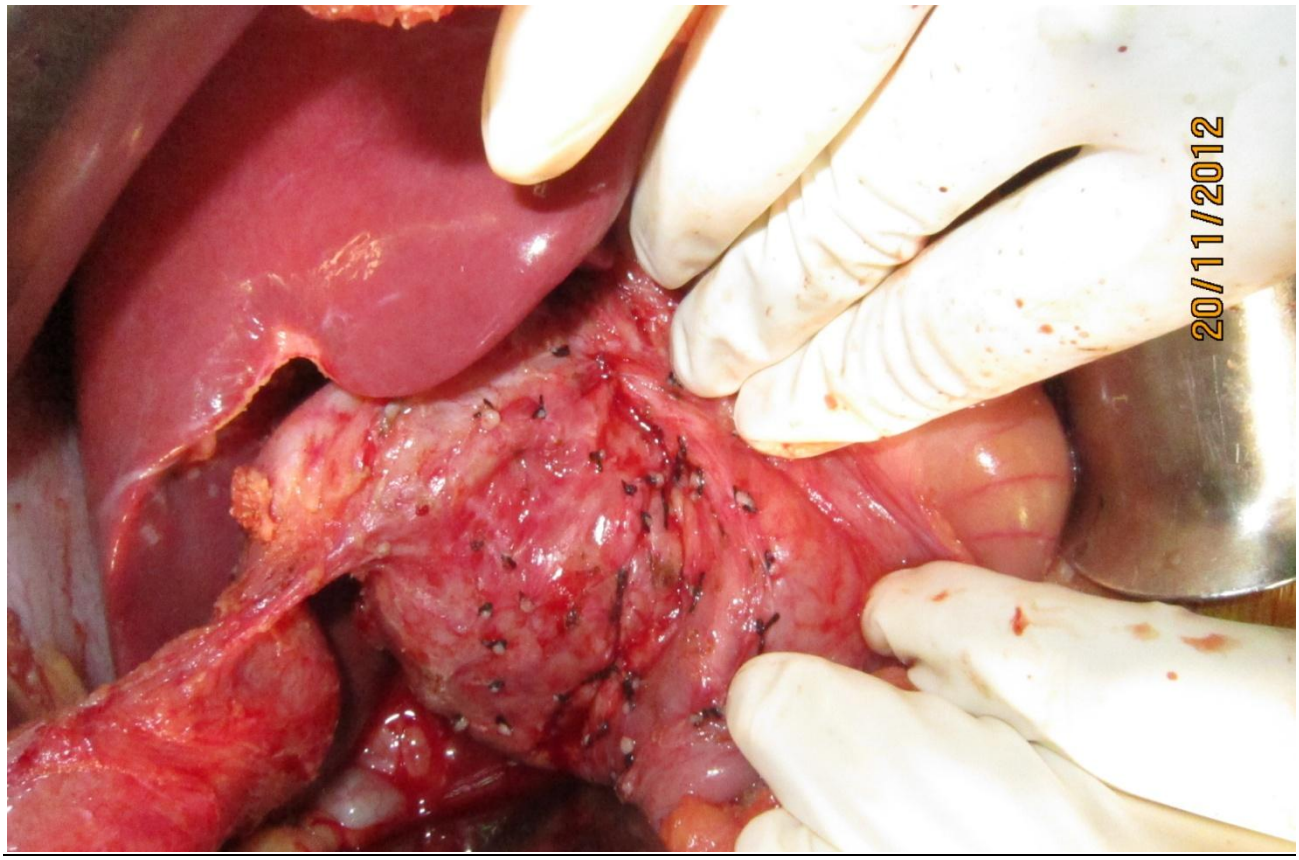


Picture 12 (Intra-operative photograph)



Type IA choledochal cyst with attached gall bladder as seen intra-operatively.

Picture 13 (Intra-operative photograph)



Another view of Type IA choledochal cyst with attached gall bladder as seen intra-operatively.

Discussion

Choledochal cysts were found to be more common in the female gender in both adults (18 out of 25) as well as children (14 out of 18). The female to male ratio among adults was 2.57:1 while among children it was 3.5:1 which was in keeping with the reported ratio in literature (3:1 to 4:1).

The most common presenting complaints were abdominal pain (96%), vomiting (48%) and jaundice/ cholangitis (20%) among adults. Among children, these were: pain (78%), jaundice (61%) and vomiting (50%). Other presenting features included pancreatitis in 2 adults and 1 child and cyst rupture with peritonitis in 1 adult. No child had the classical triad of abdominal pain, jaundice and palpable mass. Jaundice was found to be a more common presenting symptom in the pediatric age group. Similarly, the remainder of the presenting symptoms were in keeping with reports in literature. These symptoms occur as a result of bile stasis and choledocholithiasis leading to cholangitis or main pancreatic duct obstruction secondary to stones/ protein plugs leading to pancreatitis.

Associated pathology included choledocholithiasis (5 adults and 2 children), gall stones (6 adults and 1 child), pancreatitis (1 adult and 2 child), bile duct stricture (1 adult and child

each) and hepatolithiasis (1 adult). PBM is known to be associated with choledochal cyst, gall bladder (GB) cancer, cholangiocarcinoma, GB adenomyomatosis, biliary pancreatitis, non biliary pancreatitis, hilar cholangiocarcinoma, cholelithiasis, choledocholithiasis and

pancreatic cancer. The most common diagnostic modality used in the workup of these patients was ultrasound abdomen in children (97% of children and 56% of adults) and MRCP with CT abdomen in adults (88% adults and 78% children). ERCP was employed in 4 adults and 1 child; these patients presented with cholangitis. Twenty adults (80%) and 9 children (50%) underwent IOC as a part of this study.

The commonest cyst type in adults was I (68%) followed by IVA (32%) while in children it was IVA (50%) followed by I (39%). Other types were not encountered in this study. The reports in

literature have described the prevalence of the various cyst types as follows: 50%–80% type I, 2% type II, 1.4%–4.5% type III, 15%–35% type IV and 20% type V.

Long common channel (>10 mm) was seen in 13 out of 23 adults (56.5%) and 4 out of 8 children (50%). Long common channel was encountered more often in children with type I (3 out of 4) as compared to type IVA cysts (2 out of 6). No such association was seen in adults. The definition of PBM is not clear; a range from 1-4.5 cm has been described. We have taken this as >1cm. In literature, PBM is associated with choledochal cyst in 50-80% of cases and our results are in keeping with this. MRCP and IOC showed good correlation in detecting the cyst type and delineating the length of the common channel. (Correlation coefficient- 97.17%). The cyst type was well demonstrated on MRCP [22 out of 22 adults (100%) and 11 out of 11 children (100%)] as well as IOC [16 out of 17 adults (94%) and 5 out of 6 children (83%)]. However, the common channel was more frequently seen on MRCP [22 out of 22 adults (100%) and 9 out of 11 children (81%)] than on IOC [8 out of 17 adults (47%) and 1 out of 6 children (16%)]. The sensitivity of MRCP for imaging choledochal cyst has been reported to be 90-100%; that for PBM has been reported to be between 46-60% and our results have shown a higher sensitivity. However, intra-operative cholangiography fared poorly in comparison with MRCP, possibly because of the operator dependant nature of the test and because of the fact that the anatomy of the cyst may obscure the junction (e.g. large cyst overlapping the junction, cyst with stones or terminal stricture). These disadvantages are often overcome in MRCP.

Serum and bile amylase were higher in those with a long common channel. In adults with channel length <10 mm, 3 out of 8 had a bile amylase >200 U/L while among those with >10 mm channel length, 8 out of 11 had a bile amylase level >200 U/L. In children, 2 out of 3 with a short common channel had bile amylase level >200 U/L while 3 out of 4 with long common channel had a bile amylase level that exceeded 200 U/L.

A greater fraction of children (5 out of 7, 71%) had higher bile amylase (>200 U/L) levels as compared to the adults (12 out of 20, 60%). This is in keeping with literature that suggests that bile

amylase levels correlate with the degree of reflux and therefore the onset of symptoms; children present earlier due to higher amylase level in the common bile duct.

Chronic inflammation was consistently seen on histopathology. Hyperplasia (1 child, 4 adults), intestinal metaplasia (1 child, 3 adults) and biliary intraepithelial neoplasia {BilIN} (1 child and adult each), were less common.

Many genetic changes suggestive of premalignant change have been reported in patients with PBM. These include: over-expression of Ki-67, mucin core protein 1, COX 2, vascular endothelial growth factor, bcl 2, 8 hydroxy 2 deoxyguanosine as well as mutations in tumour suppressor genes such as p53 and K-ras. In this study, the cyst epithelium was studied for the presence of K-ras mutation. This was found in only two out of 36 samples while in literature, the prevalence has been described to be anywhere from 25% in non cancerous bile duct epithelium to 68.8% in cholangiocarcinoma. This may be attributed to low epithelial yield from cysts (most exhibited extensive epithelial denudation) and consequent inadequately representative samples.

The most common operation performed was hepatico-jejunostomy in adults (24 out of 25) and children (10 out of 19). End to side hepatico-duodenostomy was a close second (8 out of 19) among children. Both these operations have been described for this condition in literature.

Complications were more common in adults (15 out of 25) in the post operative period when compared with children (0 out of 18). The most common complication was bile leak (9 out of 15 adults). Other complications included secondary haemorrhage (3/15), septicemia (1/15), wound infection (2/15), anastomotic leak requiring reoperation (1/15) and gastric distension (1/15).

Bile cultures were positive in 12 out of 25 adults; culture was sterile in all the children (14 out of 14). Bile cultures were not predictive of the risk of post operative infective complications.

The drawbacks of this study include:

1. small sample size,
2. heterogeneous adult population,

3. different management protocols for adults and children,
4. inability to visualize the common channel in some intra-operative cholangiograms and MRCPs,
5. short study period (18 months) making follow up incomplete and
6. Very low prevalence of premalignant epithelial changes as well as K-ras mutation (2/42 samples).

The last could be attributed to a low yield of epithelium from cysts as most exhibited extensive epithelial denudation. Consequently, many samples may not have been adequately representative.

Conclusions

1. Choledochal cysts are more common in the female gender.

2. The common presenting symptoms are upper abdominal pain, vomiting and jaundice/ cholangitis.

3. Patients with choledochal cyst may exhibit such associated pathology as bile duct/gallbladder/ intrahepatic stones, pancreatitis and bile duct stricture.

4. Children tend to have higher bile amylase level which is in keeping with reports from literature where those who were symptomatic at an early age, had higher bile amylase level.(51)

5. The most common diagnostic modality used in these patients was ultrasonography followed by MRCP and intra-operative cholangiogram in that order.

6. The most prevalent cyst types were type I in adults and type IVA in children.

7. Long common channel was more prevalent in children with type I cysts when compared with those who had IVA cysts.

8. Long common channel was associated with higher serum and bile duct amylase levels

9. MRI and intra-operative cholangiogram exhibited good correlation in the study of the anatomy of the cyst and junction length.

10. The percentage of junctions that could be identified and measured was greater for MRI (100% adults, 81% children) as compared with intra-operative cholangiogram (47% adults and 16% children). This suggests that MRI is the imaging modality of choice in the study of pancreatico-biliary junction.

11. The most common operation after cyst excision in adults was hepatico-jejunostomy while in case of children; the numbers were almost equally divided between end to side hepatico-duodenostomy and hepatico-jejunostomy.

12. Bile cultures tended to be sterile in children and polymicrobial in adults. There was no correlation between post- operative complications and bile culture results.

13. Post operative complications were more frequent in adults as compared to children.

14. The most common post operative complication was a spontaneously resolving bile leak. Other complications included wound infection, secondary haemorrhage, anastomotic leak requiring re-operation, gastric distension and septicemia, all of which were seen only in adults.

15. Drawbacks of the study included small sample size, heterogeneous adult population, non-uniform management protocols, inability to see the common channel in some images, incomplete follow up and low prevalence of K-ras mutation.

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Annexure

PROFORMA FOR DATA COLLECTION

Name: Age: Sex: M/F

Hospital no:

Address:

Phone no:

Comorbid illness (please circle): Diabetes/ hypertension/ heart disease/

hypothyroidism/ asthma/ others (please specify).

Complaints/ problems (please circle what is appropriate):

1. Upper abdominal pain/ dyspepsia
2. Fever >100F
3. Obstructive jaundice
4. Upper GI bleed
5. Choledocholithiasis
6. Pancreatitis
7. Chronic liver disease
8. Carcinoma gall bladder/ cholangiocarcinoma
9. Incidental on imaging
10. Other (please specify)

Prior sphincterotomy: Y/N (if yes, please specify indication).

Type of choledochal cyst: IA/IB/IC/II/III/IVA/IVB/V

(MRCP/ IOC/ both)

Anomalous pancreaticobiliary junction (PBM): Present/ absent.

Type of PBM: 1a/1b/2a/2b/3a/3b/3c1/3c2/3c3

(MRCP/ IOC/ both)

Common bile duct amylase level: <200/ 200-1000/ >1000 [value: U/L]

Serum amylase level : <200, 200-1000/>1000 [value; U/L]

Dysplasia in cyst epithelium: Absent/ present (type:)

Dysplasia in proximal duct : Absent/ present (type:)

K-Ras mutation in cyst : Absent/ present (codon 12/13, type:)

K-Ras mutation in proximal duct: Present/ absent

(codon 12/13, type:)

Operation:

Findings:

Complications: Bile leak/ collection/ bleed/ septicaemia/ UTI/ LRI/ DVT/ wound Infection/ other (please specify)

[Post op day of occurrence for each:]

Outcome: Uneventful/ complication with recovery/ death

Any other comments:

PLEASE STICK THIS FORM IN THE LAST PAGE OF OUT PATIENT RECORD

IN CASE OF ANY PROBLEMS, PLEASE CONTACT SUDHINDRA. J (9894411823)

CONSENT FORM

Name: Age: Sex: M/F

Hospital No: Date of operation:

Name of operation: INTRA-OP CHOLANGIOGRAM, EXCISION CHOLEDOCHAL CYST WITH HEPATICOJEJUNOSTOMY/ HEPATICODUODENOSTOMY

With regard to the operation:

- I have been explained the indication, benefits and risks.
- I have done this in terms and language which in my judgement are suited to the understanding of the patient/ responsible relative of the patient.

Signature (with Employment number) Name of doctor

Date

Patient/ Guardian:

- I have been explained the nature of my illness, the need for and the type of operation for the same, its risks and the benefits.

I agree:

- To the proposed operation.
- To the administration of general or local anaesthesia as deemed appropriate.
- That any additional procedure if carried out will be in my best interests and justified for medical reasons.
- To the transfusion of blood or blood products if needed.
- To clinical photographs being taken and the use of fluid/ tissue from the operation for academic purposes to further medical knowledge.

Name of patient Signature (with date)

Relationship (if not patient)

PATIENT INFORMATION SHEET

The bile duct connects the liver to the intestine and it is through this pathway that bile from the liver drains into the intestine. This duct is joined by a duct with similar function from the pancreas, in the wall of the intestine (food passage). There is usually a circular band of muscle around the end portion of these ducts which closes one to the other and prevents bile from entering pancreatic duct and vice versa. Choledochal cyst is dilatation of a portion of the bile duct. This condition is believed to increase risk of cancer of the bile duct and the gall bladder. This is probably because in these patients, the bile duct is joined to the pancreatic duct outside the wall of the intestine. This means that the action of the circular band of muscles is compromised and the contents of one duct mix with the other ie, reflux of pancreatic secretions occurs into the bile duct. Pancreatic secretions are rich in digestive juices that act directly on the bile duct and cause irritation and damage. This damage is repaired by the body. Over a prolonged period of time, this cycle of repeated damage followed by repair is believed to lead to cancer in a stepwise manner. Therefore, the current prescribed treatment for such patients is removal of the dilated portion of the bile duct and joining the remainder of the duct to a portion of the intestine. The following steps will be undertaken during the course of this operation:

1) Cholangiogram (injection of a dye into the bile duct during the operation and a X ray of the abdomen. This delineates the ductal system).

2) Aspiration of bile using a syringe and needle during the operation and testing for the level of amylase (a substance in pancreatic juice). We will anyway aspirate bile at the time of operation to look for microbes in the bile.

3) Looking at changes in the removed cyst and a portion of the liver under a microscope and looking for the presence/ absence of an abnormal form of a gene called k-ras (gene: the portion of the cell that codes for its growth and multiplication).

Complications of the operation include the following:

1) Bile leak from the junction of bile duct and intestine.

2) Bleeding during and after the procedure.

3) Infection- within abdomen, of the chest/ wound/ urine/ blood.

4) Possible need for reoperation/ radiological drainage procedure in case of 1).

5) Pain/ scar on the abdomen.

Data sheet

NAME		NUMBER	CLINICAL DATA	IMAGING	CYST TYPE	CYST TY
					MRI	CHOLAN
Adrita Das	F	036855F	ruq pain 2/12, cholangitis 1 episode	USG, IOC	NA	Type 1
Nishta Kumari	F	018667F	ruq pain, jaundice, vomiting 3yrs	USG, MRI	Type 1	NA
Pampa Lal	F	980202D	upper abd post prandial pain, vomiting 2yrs	USG, IOC	NA	Type 4A
Smriti Dutta	F	953163D	ruq pain, vomiting 3yrs, pancreatitis, distal CBD stricture choledocholithiasis	USG, IOC, MRI	Type 4A	NA
Deepak Kumar	M	938438D	abd pain 1/12	MRCT	Type 1	NA
Anisha Pal	F	829657D	jaundice, gallstones, loose stools 1 episode	USG, IOC	NA	NA
Sivani Kumari	F	802549D	epigastric pain, vomiting, fever, obstructive jaundice 3 years- cholangitis	USG, IOC	NA	Type 4A
Shakshi Singha	F	827064D	obstructive jaundice 3/12	USG, IOC	NA	not seen
Abraham	M	852185D	upper abd pain, vomiting, obstructive jaundice 10 days	USG, IOC	NA	Type 4A
Sonam Choki	F	855458D	ruq pain, fever, jaundice 1 wk, 1 month ago- cholangitis	USG, IOC	NA	Type 1
Dharshini	F	085385F	ruq pain, vomiting 6/12	USG, MRCT	4A	NA
Seona	F	722824D	upper abd pain, vomiting, choledocholithiasis, pancreatitis1- ERCP+stent 9/12 ago	USG, MRI, ERCP	4A	not seen
Nandu	F	046401F	ruq pain, vomiting, fever, jaundice 5 days- cholangitis	USG, MRCT	Type 1	NA
Ankush Maity	M	031357F	ruq recurrent pain for 6 yrs	USG, MRI	Type 1	NA
Suvro J Saha	M	061209F	obstructive jaundice 6/12	USG, MRI	4A	NA
Amrita kumari	F	081421F	ruq pain, vomiting 8yrs. Jaundice 5/12	USG, IOC, MRCT	Type 1	NA
Vijaya's baby	F	092153D	ruq pain, fever, jaundice 2 weeks- cholangitis	USG, MRCT	4A	NA
Krittika Gupta	F	209065F	upper abd pain, fever, vomiting 6/12	USG, MRCT	4A	NA
?Anita Devi#	F	969166D	ruq pain 2 ep in 7 yrs. Lap chole for gallstones, choledocholithiasis	MRCT, IOC	NA	Type 4A
Saritha#	F	065955D	ruptured cyst with peritonitis antepartum	USG, MRCT, IOC	Type 1	Type 1
Pushpa John	F	836842D	one episode ruq pain	MRCT, IOC	Type 1	Type 1
Lalngaihzuali	F	886106D	dyspepsia, lower abd pain 20 yrs, choledocholithiasis, CBD stricture, ERCP#	USG, MRCT, IOC	Type 1	Type 1
Radha Sundari	F	684776D	cholangitis, choledocholithiasis, sphincterotomy#	USG, IOC	NA	Type 1
Patubala Kumari	F	850932D	ruq pain 11 yrs, open chole done for gallstones	USG, MRI	Type 1	NA
Josna Rani Das	F	865380D	ruq pain, jaundice, vomiting, gallstones. open chole- bile leak	MRI, IOC	Type 1	not clear
?Chabi Rakshit	F	792178D	ruq pain one episode, vomiting, gallstones	USG, MRI, IOC	Type 1	not clear
Meenakshi Devi	F	982175D	recurrent ruq pain 14 yrs, vomiting, cholangitis 1/12, ERCP unsuccessful	MRCT	Type 4A	NA
Rehena Bibi	F	934335D	ruq pain, vomiting 3 yrs	USG, IOC	NA	Type 4A
Ashok Mahata	M	926832D	ruq pain 15 yrs	MRCT	Type 1	Type 1
Minu Rani Bera	F	885660D	ruq pain and vomiting 2yrs	USG, MRI, IOC	Type 1	Type 1
Aruna Mondal	F	935066D	ruq pain 5 yrs, melaena 1 episode	MRCT, IOC	Type 1	not seen
Kolappa Pillai	M	039261F	ruq pain, vomiting one episode	USG, MRCT, IOC	Type 1	Type 1
Gouri Ghosh	F	081437F	ruq pain 2yrs	MRCT, IOC	Type 1	Type 1
Lakshmi	F	443644D	epigastric pain 4/12, gallstones- lap chole	USG, MRCT, IOC	Type 1	NA
Sajid Hussain#	M	485571D	ruq pain 8 yrs, vomiting, gallstones, hepatolithiasis, sphincterotomy#	MRCT, IOC	Type 4A	Type 4A
Bankim Chandra	M	708764B	ruq pain 2 yrs	USG, MRCT	Type 1	NA
Perumalsamy#	M	753359D	ruq pain, fever, choledocholithiasis, sphincterotomy#	USG, MRCT	Type 4A	NA
Tika Sharma#	F	757669D	recurrent cholangitis, gallstones	MRI, IOC	Type 4A	Type 4A

Data sheet (continued)

YPE	JUN LENGTH	JUN LENGTH	JUNCTION TYPE	JUNCTION TYPE	TB/DB	ALP	CA 19-9	AMYLASE (SERU	LIPASE (SERUM	AMYLASE (E	LIPASE (BILE
IGIC	MRI	CHOLANGIO	MRI	CHOLANGIO							
	NA	not clear			0.6/0.2	173		not done	not done	-	-
	9 mm	NA			0.4/0.1	280		76	66	12600	17248
	NA	not clear			0.4/0.1	304		93	-	1887	8823
	4 mm	NA			0.4/0.1	254		158	-	unsuitable	unsuitable
	14 mm	NA			0.6/0.1	291	<2.5	76	35	13500	33700
	NA	NA			0.7/0.1	291		88	125	10	26
	NA	not clear			0.5/0.2	315		142	53	20500	103950
	NA	not seen			7.3/6.4	1201		296	417	21	-
	NA	2 mm			2.0/1.7	253		79	-	<10	-
	NA	not clear			0.4/0.2	208		286	112	12613	73549
	9 mm	NA			0.6/0.2	186		212	104	10863	78790
	18mm	not seen			0.5/0.1	176		242	33	68900	375500
	13mm	NA			0.7/0.5	243		177	142	-	-
	not clear	NA			0.4/0.2	241		97	43	-	-
	not clear	NA			2.1/1.8	469		-	-	-	-
	11mm	NA			0.4/0.1	228		60	19	93	414
	16.3mm	NA			4.3/3.3	503		241	191	15000	103400
	7.5mm	NA			0.5/0.2	307		not done	not done	not done	not done
	NA	6 mm			0.4/0.1	61		-	-	100200	123400
	6 mm	7 mm			0.4/0.1	85		1740	2236	40	1203
	6 mm	5.6 mm			0.5/0.2	140	<2.50	-	-	116400	1006000
	23 mm	26 mm			0.4/0.2	80	3.92	345	163	9310	12210
	NA	not clear			0.4/0.2	97		123	61	18	132
	5 mm	NA			0.4/0.1	127		-	-	-	-
	9 mm	not clear			0.6/0.4	431		-	-	6	34
	13 mm	not clear			0.4/0.1	106		51	54	5	24
	13 mm	NA			5.6/4.5	394		-	-	92	55
	NA	not clear			0.5/0.1	65		-	-	20	12
	22 mm	26 mm			0.7/0.2	103		48	19	65800	112100
	5 mm	4 mm			0.4/0.1	90				LOW	21
	14.5 mm	not seen			0.5/0.1	88		-	-	36800	-
	19 mm	29 mm			1.5/0.1	51		324	515	4200	14800
	10mm	15mm			0.5/0.2	101				34730	163690
	2mm	NA			0.5/0.1	111		135	74	-	-
	7mm	not seen			0.6/0.2	74		-	-	12	91
	8mm	NA			1.4/0.7	212		-	-	68	37
	7mm	NA			1.1/0.3	60		305	235	-	-
	19mm	not clear			0.4/0.1	265		173	219	118	1027

Data sheet (continued)

CULTURE	PATHO CHANGES	SLIDE NO	K RAS MUT	OPERATION	FINDINGS	OUTCOME
no growth	inflammation	HA5, lower end		hep jej		recovered
no growth	pyloric metaplasia	focal pyloric gland metapl: B2, 3 & C2		hep jej		recovered
no growth	inflammation	B-E, not marked		hep duo		recovered
no growth	inflammation	HD complete, E part		hep jej		recovered
no growth	inflammation	HB2, B4		hep jej		recovered
no growth	inflammation	HA3		hep duo		recovered
no growth	inflammation	HA, F2		hep duo		recovered
-	inflammation	B2, F, E prox end		hep jej		recovered
no growth	inflammation	HC1 prox, C ulceration		hep duo		recovered
no growth	inflammation	completely denuded		hep duo		recovered
no growth	inflammation	HB2, B3		hep jej		recovered
no growth	inflammation	not mentioned		hep jej		recovered
-	inflammation	HB2		lap hep duo		recovered
-	micropap h'sia	micropap h'sia. HA1/ A3-A5		hep duo		recovered
-	BilIN-1	HB1/B2		hep jej		recovered
-	inflammation	HA1-A2. A5 cys duct resection margi		hep jej		recovered
no growth	inflammation	AFB1-3, not marked		hep duo		recovered
not done	inflammation			hep jej		recovered
no growth	inflammation	HA5		hep jej		bile leak, washout+transanas stent
no growth	inflammation	not marked		hep jej		recovered
Enterob, E coli	inflammation	not marked		rad chole hep jej		bile leak, collection- pigtail, consol
Citrob, Enteroc, Kleb	focal microp, intes	HA5, A6 micropap h'sia		hep jej, stone removal		bile leak
no growth	inflammation	B more, C complete, D focal		hep jej		redo jj, hep jej stenting
no growth	inflammation	A3>A4		hep jej		bile leak
E coli	inflammation	HA3, 4		hep jej		bile leak, bleed around drain
No growth	inflammation	HB1, 2		hep jej		bile leak, melaena
no growth	inflammation	not marked		hep jej		wound infection
E coli	micropap	C3>C1		hep jej		fever
no growth	bilIN	Focal bilIN A3>A2,5		hep jej		bile leak
no growth	intes metaplasia	C1		hep jej		bleed into drain
Aeromonas	micropap	A3>A4		hep jej		bile leak, wound infection
no growth	inflammation	HB2-B4 (B3-4better)		hep jej		recovered
E coli, Enteroc	inflammation	HB2, distal margin also has epitheliur		hep jej		recovered
no growth	inflammation	HA3>A2		hep jej		recovered
Enteroc, E coli, Citrob, Pseu	inflammation	not marked		hep jej		recovered
E coli, Enteroc+b, Aerom	micropap, intes meta	D and E		hep jej		recovered
Enteroc, E coli, Aerom	inflammation	HA2		hep jej		gastric distension
E coli, Enteroc, Citrob	micropap	A1-3, A3 focal micropap h'sia		hep jej		recovered

Data sheet (continued)

Moumita Mandal	F	793742D	Epigastric pain one episode, vomiting	USG, MRCT, IOC	Type 1	Type 1
Srinivasan	M	930649D	ruq pain, vomiting 2 episodes	USG, MRCT, IOC	Type 4A	Type 4A
Neha Verma	F	939635D	ruq pain 17 yrs, pancreatitis chronic	MRCT, IOC	Type 4A	Type 4A
Taba Lucky	M	991924D	cholangitis one episode	MRCT, IOC	Type 1	Type 1
Chayagiri	F	152625F	cholangitis one episode	USG, MRCT, IOC	Type 1	Type 1

	16mm	not clear			0.4/0.1	85		-	-	47800	-
	43mm	49mm			1/0.3	88		267	219	-	-
	18.6mm	not clear			0.5/0.2	107		-	-	84500	40900
	16mm	21mm			3.3/2.6	148		-	-	104500	67900
	15mm	24mm			0.4/0.2	123		267	436	10900	72800

no growth	inflammation	HA3-5		hep jej		recovered
Klebsiella	inflammation	B3		hep jej		recovered
no growth	inflammation	C1,3		hep jej		bile leak
no growth	inflammation	HA4		hep jej		recovered
Klebsiella	inflammation	BFB 1, B2		hep jej		vomiting, tachycardia- septicemia

Clinical audit

Introduction

Diabetes is a major public health problem in India and its prevalence continues to be on the rise. According to the Fourth Diabetes Atlas of the International Diabetes Federation (IDF), there were approximately 50.8 million cases in India in 2010 while by 2030; this is expected to be 87 million. It is estimated that the increase in the number of patients with diabetes in the developing world will thrice as much as that in the developed world.(1) Mohan et al estimated the prevalence of diabetes in South India to be 8.3% in 1989 which rose to 14.3% (72.3% increase, $p<0.0001$) by 2000. The age at diagnosis also showed a downward trend.(2) Misra et al observed the rate of increase of prevalence to be greater in males as compared to females in rural India.(3) By 2030, India, Pakistan and Bangladesh are expected to occupy three of the top ten slots in diabetes prevalence in the world.

Patients with diabetes remain asymptomatic till they develop severe target organ damage (retinopathy, nephropathy, neuropathy, cardiovascular disease). Diabetes is the leading cause of blindness and kidney failure and the 6^{th} leading cause of mortality worldwide.(4) Therefore, effective screening and management strategies to combat this epidemic are the need of the hour.

This study aimed to evaluate the completeness of evaluation of diabetes and recommendations offered to patients admitted in a General Surgery unit in a tertiary hospital in South India in the last year.

Objectives

To check if the following were included in the diagnostic workup of all patients with diabetes admitted in Surgery 4 between December 2011 and November 2012:
1. HbA1c
2. Fasting lipid profile
3. Creatinine
4. Either of UP/UC, urine microalbumin or 24 hr urine protein to assess proteinuria
5. Documented examination of peripheral pulses
6. ABPI with toe pressure
7. Evaluation by Endocrinologist and counselling by diabetic educator

To check if the following recommendations were included in the discharge summary of the above patients
1. Lifestyle changes: diet, exercise and foot-care
2. Low dose Aspirin
3. Statin

Materials and methodology

This was a retrospective cohort study involving online survey of Surgery 4 discharge summaries (Dec 2011- Nov 2012) to identify patients with diabetes and study the above mentioned parameters. Results were analysed by Chi square test for significance.

Inclusion criteria

All patients admitted in Surgery 4 between Nov 2011 and Oct 2012 with the words 'Diabetes' or 'Diabetes mellitus' or 'Diabetic... (foot/abscess/ulcer etc)' in the diagnosis column of the discharge summary.

Exclusion criteria

1. Patients who died during treatment or were discharged against medical advice.
2. Readmission in the same year (only first admission counted).
3. Patients who have been advised diet regulation alone.
4. Where the discharge summary does not mention the diabetic status of a patient.

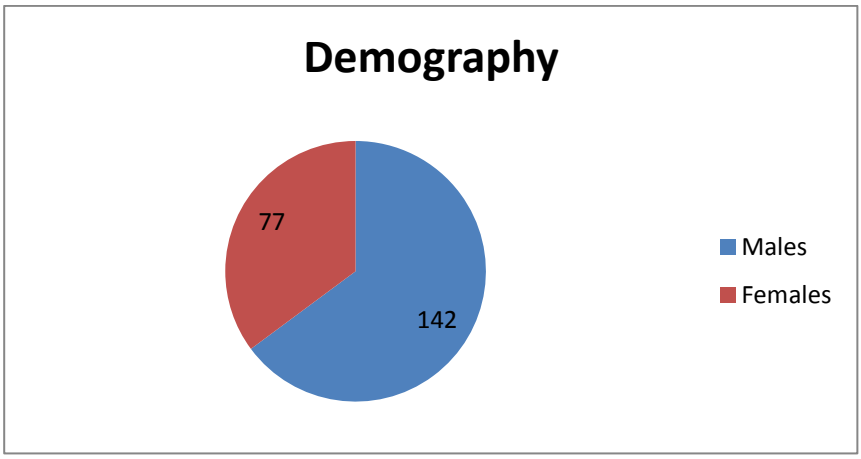
Criteria/ standards used

The American Diabetes Association (5) and American Association of Clinical Endocrinologists (6) guidelines were used as a benchmark for data collection. The ideal rate of compliance was taken as 100%.

Results

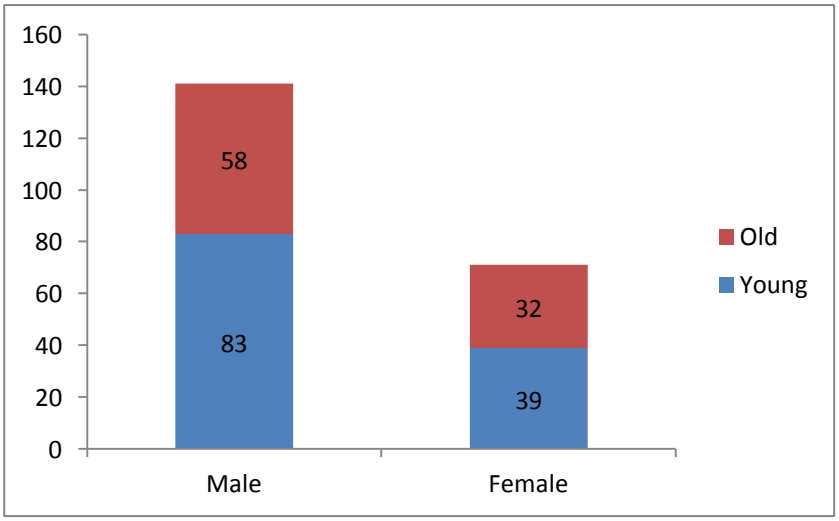
1. **Demographic profile**

There were a total of 212 patients who were included; 142 were male and 77 were female.



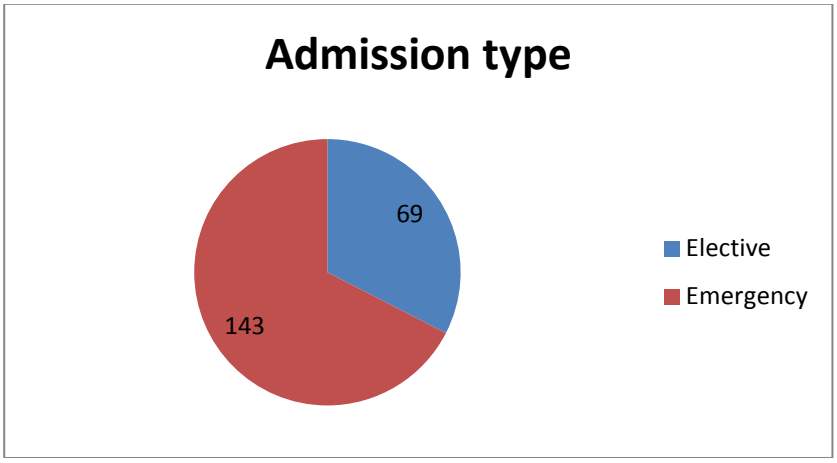
2. **Age distribution**

Patients were classified as young (<60 yrs) or old (60 yrs or more). The young outnumbered the old among both males and females. (p=0.58). (Range 27-84 years).



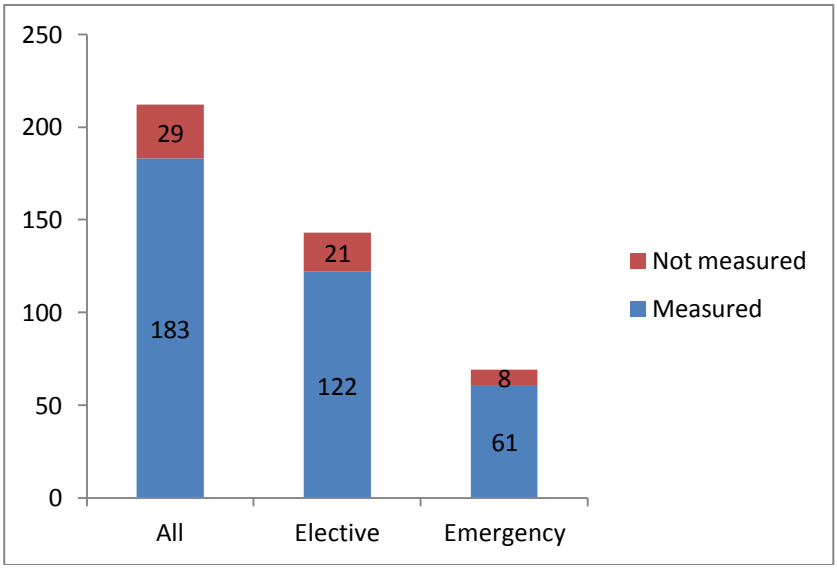
3. Type of admission

Admissions were classified as elective or emergency for further analysis. Emergency admissions were more common than elective.



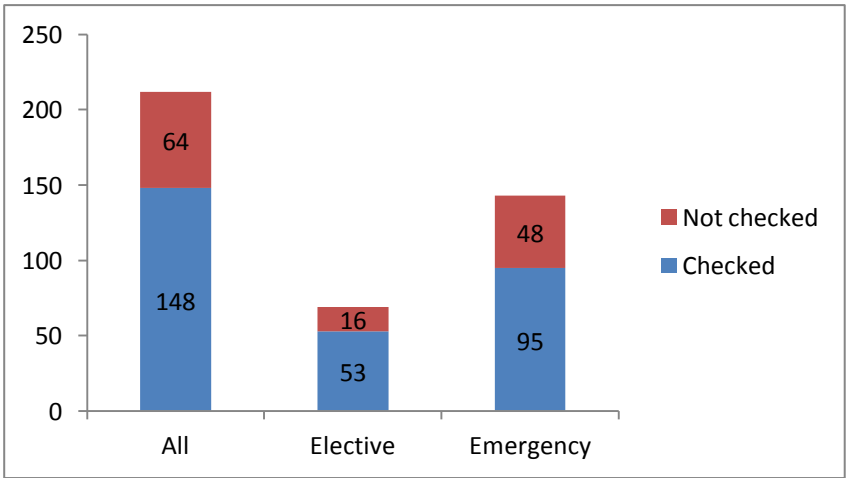
4. HBA1c

Glycated haemoglobin was measured in 86% patients. The respective percentages for elective and emergency admissions were 88 and 85%. (p=0.54).



5. Fasting lipid profile

Fasting lipid profile was checked in 148 out of 212 patients (69.8%) of which 95 out were emergency and 53 were elective admissions. In other words, lipid profile was checked in 66.4% emergency and 76.8% elective admissions. (p=0.12).

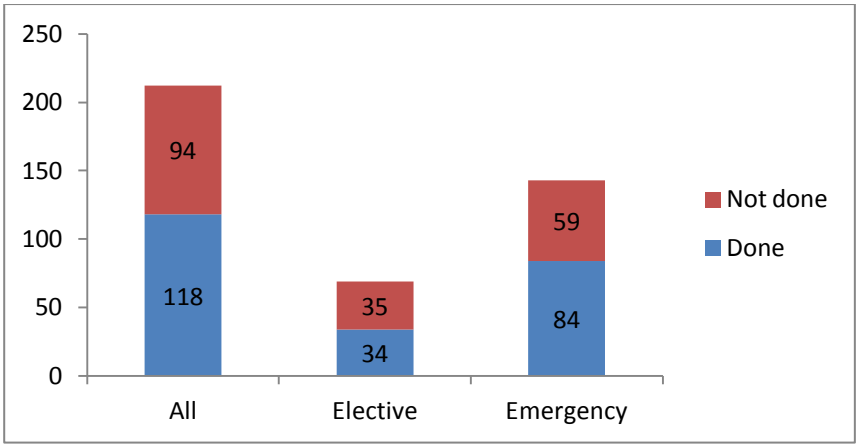


6. Creatinine/ GFR

This was measured in all patients, probably as a mandatory requirement for an operation.

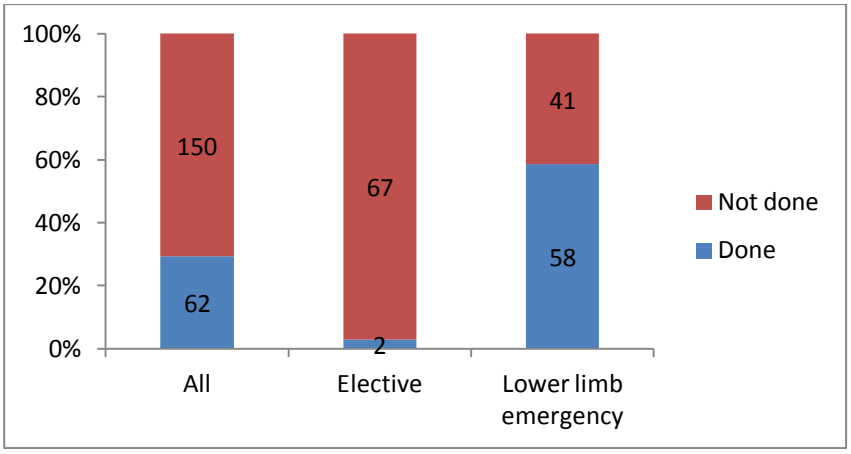
7. Evaluation of proteinuria

Either of urine microalbumin/ urine protein to Creatinine ratio/ 24 hour urine protein was employed to evaluate proteinuria. This was done in 118 out of 212 admissions (55.7%). (p=0.19)



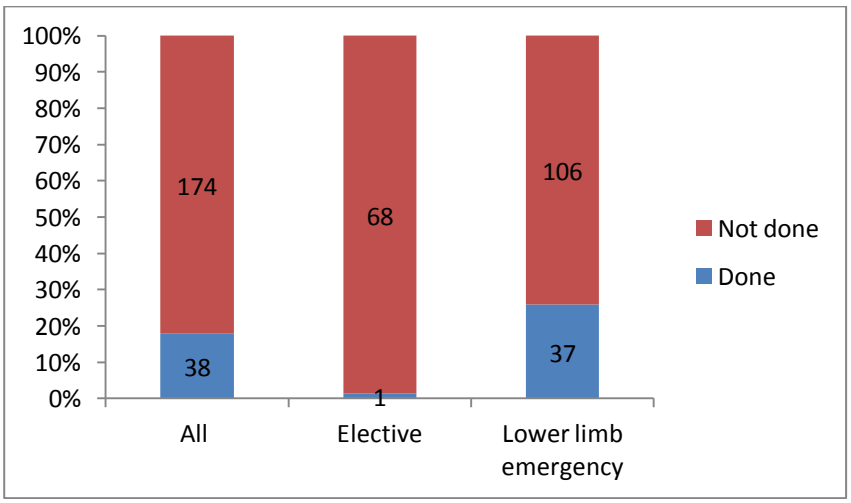
8. Palpation of peripheral pulses

This was done in only 62 out of 212 admissions (29.2%). However, if only patients admitted for emergency operations on lower limbs were studied, this percentage was higher (58.6%) when compared with elective admissions (2.9%). **(p= <0.000001)**.



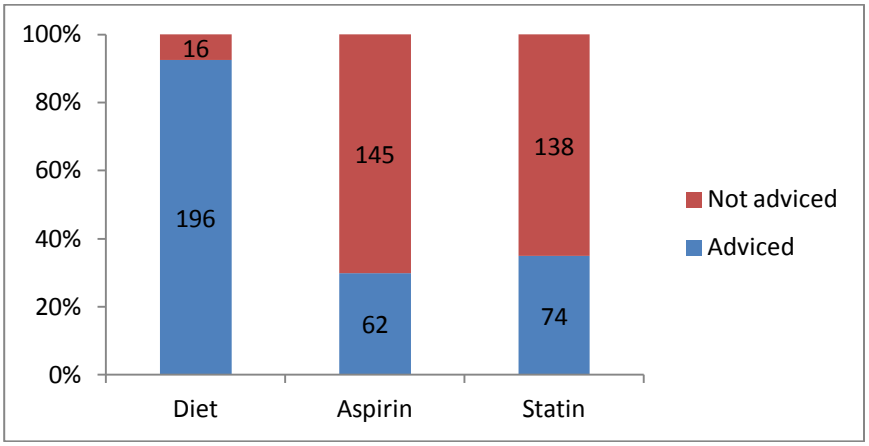
9. ABPI measurement

Measurement of the ankle-brachial pressure index with toe pressure was carried out in 38 admissions (17.9%) out of which, the majority were in those undergoing emergency lower limb operations (37/ 38). **(p=0.0001)**.



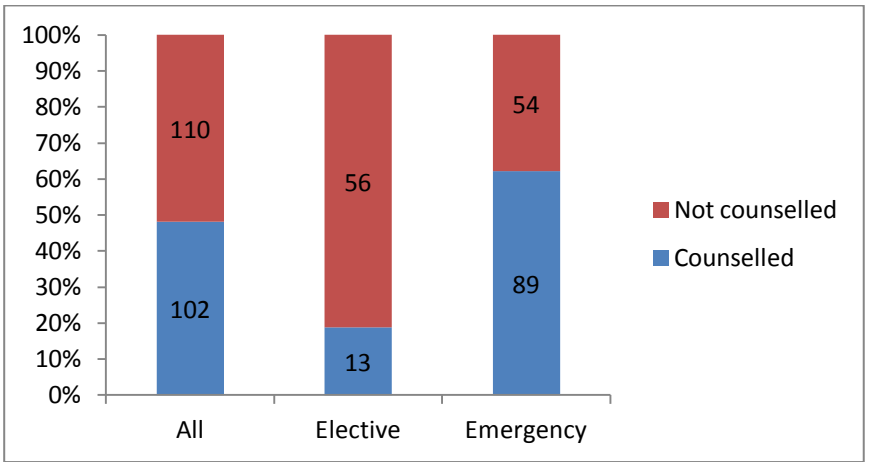
10. Recommendations

This included advice on diet, exercise, low dose Aspirin and statin. Diet advice was offered to 92.4% patients (94.4% emergency, 88.4% elective, p=0.12). The rates for Aspirin and statin were 29.9% (33.6 emergency, 20.2% elective, **p=0.05**) and 34.9% (38.5% emergency, 27.5% elective, p= 0.11) respectively. Most patients in our country are at increased risk for cardiovascular disease (4) and many have additional risk factors (50% in the present study) and would qualify for pharmacotherapy in addition to lifestyle modifications.



11. Education

Evaluation by Endocrinologist and/ or counselling by certified diabetic educator during the course of inpatient admission were achieved in 48.11%. The rates for elective and emergency admissions were respectively, 18.8% and 62.2% (**p <0000001**).



Conclusions

1. Most patients admitted to Surgery 4 in the last year were young males and the nature of admission was an emergency.
2. Creatinine (100%), HBA1c (86%) and lipid profile (69.8%) was measured in a higher percentage of patients.
3. Proteinuria (55.7%), palpation of pulses (29.8%) and ABPI measurement (17.9%) were less frequently carried out.
4. Diet advice was given to most (92.4%) while diabetic education (48.11%), Aspirin (29.9%) and statin (34.9%) were given to a smaller fraction.
5. Patients admitted for emergencies were on the whole; better evaluated and advised as compared to elective admissions (significant in case of pulse palpation, ABPI measurement, diabetic education and low dose Aspirin recommendation). This may be because they have greater end organ damage which comes to the attention of the treating physician and because patients with lower limb emergencies require evaluation of distal vascularity.

Recommendations

1. To manage all diabetic patients based on a protocol with a clinical checklist, in keeping with ADA/AACE guidelines.
2. Better evaluation of peripheral pulses and ABPI, especially among those admitted for elective operations is required.
3. Diabetic diet/ pharmacotherapy recommendations have to be studiously implemented in all patients. In the same vein, a plan for continuing review with Endocrinologist/ diabetic educator has to be made in consultation with the patient at discharge.

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